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Original research

MULTIDISCIPLINARY IN TREATMENT OF BRAIN GLIOBLASTOMA: THE COMBINATION OF SURGERY, RADIOTHERAPY AND CHEMOTHERAPY

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ABSTRACT

Objectives: *To describe the clinical features and magnetic resonance imaging of cerebral glioblastoma. And to evaluate the results of surgery combined with radiotherapy and chemotherapy for the group of patients.*

Methods: *A case series study was conducted on 38 patients with brain glioblastoma who underwent microsurgery combined with radiochemotherapy and Temozolomide at a dose of 75mg/m^2 daily and maintenance chemotherapy with Temozolomide at a dose of 175mg/m^2 for 6 cycles at Hue Central Hospital during 9/2019 - 6/2023.*

Results: *The mean age was 54.5 ± 10.3 with the male/female ratio = 1.57. The location was mainly in frontal lobe (26.3%). The tumor size 3 - 5 cm accounted for 50% of the patients. Magnetic resonance imaging showed mixed structures (47.4%) and heterogeneous enhancement (94.7%). Most patients underwent partial resection (65.8%). The main radiation dose was 59.4gy - 60gy, the patients with IMRT radiotherapy technique accounting for 23.7% After treatment treatment, the percentage of patients with symptoms such as headache and nausea reduced by about 30%. Partial response accounted for 50% of cases. The mean progression-free survival was 10.2 ± 1.06 months. The mean overall survival was 19,9 ± 1,84 months.*

Conclusion: *Glioblastoma was a highly malignant and rapidly progressive. Combination of radiotherapy and chemotherapy after surgery improved symptoms and increased overal survival.*

Keywords: *Glioblastoma, multidisciplinary treatment.*

I. BACKGROUND

Glioblastoma is a primary tumor of the central nervous system, originating from neuroglial cells, which develop mainly from the astrocytes. According to the World Health Organization (WHO), it has the highest malignant degree (grade 4) [1].

The rate of glioblastoma is quite high, accounting for about 12 - 15% of intracranial tumors and 60 - 75% of astrocytomas. In the US, the incidence is about 2.96 new cases/100.000 people/year [2]. In the UK, glioblastoma occurs in 7.36/100,000 people and the most common age group is 50 - 59 (Baker 1976). In Vietnam, some authors investigated investigate glioblastoma include: Hoang Minh Do (2009), the rate of glioblastoma in the brain was 17.2%; Kieu Dinh Hung (2006) the rate is 62.7%; Hoang Van Manh (2013) rate 45.3% [3 - 5].

Glioblastoma treatment includes 3 main methods: tumorectomy, radiotherapy and chemotherapy [9]. Currently, many centers are applying new radiotherapy techniques and new treatment drugs, combining many methods to improve treatment effectiveness and improve the quality of life for patients. For many years, Hue Central Hospital has applied multidisciplinary treatment and high-tech radiotherapy in brain tumors, especially glioblastoma. Therefore, we conducted this research to evaluate the results during the recent treatment period.

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II. SUBJECTS AND METHODS

We retrospectively analyzed 38 glioblastoma patients receiving multimodality treatment at Hue Central Hospital from September 2019 to June 2023

Steps for data collection: Glioblastoma patients underwent microsurgical tumor removal surgery at the Department of Neurosurgery, then were transferred to the Department of Radiation Therapy - Oncology Center to undergo radiotherapy combined with oral doses of Temozolomide 75mg/m^2 daily, then maintained chemotherapy Temozolomide 175mg/m^2 for 6 cycles and follow up every 3 months. All patients had a MRI and clinical symptom monitoring at each follow-up visit. RECIST 1.1 criteria is used to assess response.

III. RESULTS

3.1. Clinical and subclinical characteristics

The average age was 54.5 ± 10.3, gender ratio male/female = 1.57. Reasons for hospitalization included headache (86.8%) and hemiplegia (52.6%). Interval time from first symptom onset to hospital admission mainly less than 1 month (50%). Patients had Karnofsky score mainly from 70% - 90%.

Table 1: Onset clinical signs

Sign	N	Rate (%)
Headache	33	86.8
Vomit	10	26.3
Dizzy	8	21.1
Blurred vision	9	23.7
Mental disorder	5	13.2
Speech disorder	4	10.5
Epileptic	9	23.7
Hemiplegia	20	52.6
Memory decline	17	44.7
Total	38	100

Headache accounted for 86.8%, the others signs were under 50%

3.2. Imaging

Table 2: MRI Imaging

Result		N	Rate (%)
Location	Frontal lobe	10	26.3
	Parietal lobe	3	7.9
	Occipital lobe	4	10.5
	Midline	4	10.5
	Posterior fossa	7	18.4
	Multiple lobe	7	18.4
Dimension	< 3cm	12	31.6
	3 - 5cm	17	44.7
	> 5cm	11	28.9
Component	Solid	6	15.8
	Cyst	14	36.8
	Mixture	18	47.4
Contrast enhancement	No	3	15.8
	Homogeneous	2	5.3
	Heterogeneous	36	94.7
	Marginal enhancement	25	65.8
Necrosis	Yes	21	55.3
	No	17	44.7
Midline shift	Yes	9	23.7
	No	29	76.3
Haemorrhage	Yes	20	52.6
	No	18	47.4
Edema	No	2	5.3
	Grade I	14	36.8
	Grade II	15	39.5
	Grade III	7	18.4

The most frequency tumor location was in frontal lobe (26.3%) and multiple lobe (18.4%). 44.7% patients had tumor's size 3 - 5cm. 40% tumor's component was cyst and mixture. 94.7% tumor present heterogeneous enhancement on MRI. Necrosis and haemorrhage accounted for more than 50%. Grade II edema rate was 39.5%.

3.3. Treatment characteristics

Table 3: Type of surgery

Type of surgery	N	Rate (%)
Total tumorectomy	9	23.7
Partial tumorectomy	25	65.8
Tumor biopsy	4	10.5
Total	38	100

Most of patient underwent partial tumorectomy (65,8%)

Table 4: Radiotherapy characteristics

Result		N	Rate (%)
Dose	35gy/10Fx 59.4gy/33fx 60gy/30fx	8 14 16	21.1 36.8 42.1
Technique	IMRT/ Vmart 3D	9 29	23.7 76.3
Number of 3D field	2 3 4	12 17 9	31.6 44.7 23.7

Two third patients received radiotherapy dose from 59.4 to 60 Gy. IMRT accounted for 23.7%. 2 radiotherapy field rank first with 44.7%.

Table 5: Radiotherapy adverse affects

Adverse affects	N	Rate (%)
Hair loss	25	65.8
Vomit, nause	17	44.7
Anorexia	21	55.3
Fatigue	31	81.6
Otitis	3	7.9
Total	38	100

On top of the list was fatigue with the rate of 81.6%. The next frequent adverses affected hair loss, anorexia and vomit, nause with the figures around 60%.

3.4. Response evaluation

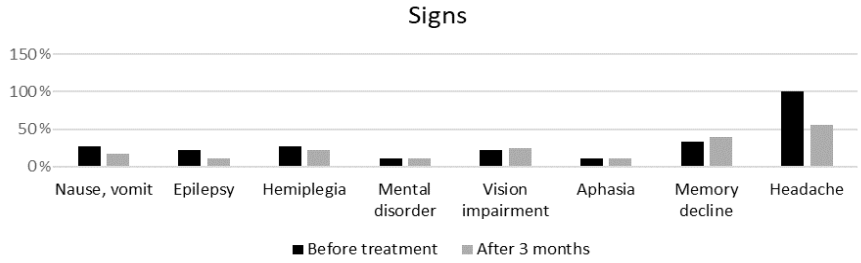


Figure 1: Clinical improvement after 3 months

After treatment, headache and nause eliviated by approximately 30%. Memory and vision impairment was more serere by nearly 10%.

Table 6: Response evaluation on MRI

Response rate	N	%
Complete response	3	7.9
Partial response	17	44.7
Stable disease	12	31.6
Progression	6	15.8
Total	38	100

Partial response rank first by 44.7%. The second belong to stable disease with 31.6%.

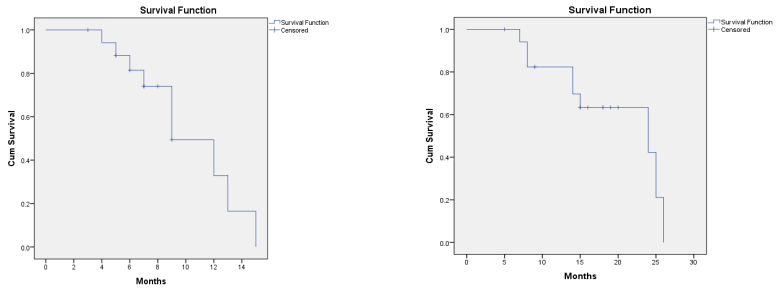


Figure 2: Progression free survival and overall survival

PFS was 10.2 ± 1.06 months and OS was 19.9 ± 1.84 months.

IV. DISCUSSION

4.1. Clinical features

In our study, the average age of patients was 54.5. Our research results were consistent with the one of Hoang Minh Do (2009) that the most common age group was ≥ 40 years old, accounting for 59.3%. Hoang Van Manh (2013) also state that the most common age group was over 50 years old, accounting for 25.3% [3, 4].

Regarding gender, in our study, the disease was more common in men than in women with the figures is 61,1% and 38,9% respectively. This result was similar to the results of Dong Van He (2013), Hoang Minh Do (2009) with 60% male and 40% female [3, 6].

According to Bajcsay and colleagues: High degree malignant gliomas had a rapid growth time, 70% - 80% was less than 3 months [7]. Headache symptoms: According to our results, headache was a common symptoms of glioblastoma, accounting for 86.8%. This is also a symptom of brain tumors in general. This result was consistent with the results of Hoang Van Manh that headache was encountered in 92% of patients [4]. Headache symptoms occurred in 96% of Muller's study [5]. Increased intracranial pressure: Symptoms include headache, vomiting, and papilledema. This is the specific clinical sign of intracranial mass. In our study, vomiting occurred in 26.3%, vision impairment occurred in 23.7%. According to Wiegrat, increased intracranial pressure syndrome is common in the tumor group.

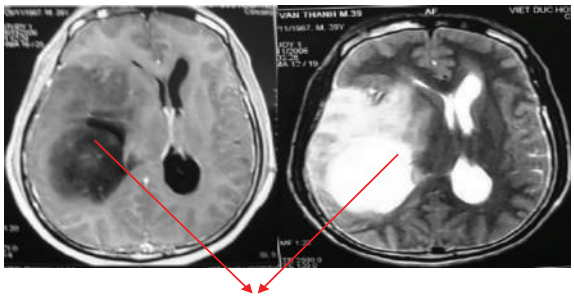
4.2. Imaging features

Glioblastoma is the brain tumor with the highest malignancy, the diagnosis based on MRI usually has high accuracy. This type of tumor has many cysts in the tumor, producing irregular hyperintensity on T2 Flair, extensive cerebral edema around the tumor.

About the location: Frontal lobe and multiple lobes accounted for 26.3%, the others were in other areas. According to Hoang Minh Do, the most common tumor location was the temporal region (33.1%), followed by the frontal area (26.9%) [3]. Kieu Dinh Hung studied the group of malignant gliomas and found that the frontal area was found by 41.9% [5]. Hoang Van Manh stated that tumor in the temporal region was found in 30.7% and in the forehead was 29.3% [4].

In our study, tumors with a large size of 3-5cm accounted for the highest rate (44.7%), tumors with a size of > 5cm accounted for 16.7%. According to Ali Mehdi Ayoub, in France, 72% of patients with malignant glioma were diagnosed with tumor diameter less than 5cm [8], Yabroff KR showed that 81% of malignant glioblastoma and less differentiated astrocytoma tumor diameter from 2 - 5cm [9].

Tumor intensity in T1W, T2W



Brain tumor

Figure 1: MRI show that the tumor hypointense in T1W, hyperintense in T2W, cerebral edema, grade II midline shift

4.3. Degree of invasion and pressure on surrounding tissues

The phenomenon of the tumor pressing on surrounding tissues is due to the size of the tumor itself and brain edema. The larger the tumor size, the more brain edema causes the more severe compression. This feature is common in high-grade malignancies. Images of compression appear on computed tomography and magnetic resonance imaging: collapsed, dilated ventricles, midline shift and deformation of the entire brain lobe. In our study, the tumor caused edema: grade II accounted for 36.8%, grade III accounted for 39.5%.

4.4. Surgical results (Based on the method of surgery)

In this study, the majority of cases had partial tumorectomy (66.7%), 16.7% of cases had the entire tumor removed. Patients underwent surgery to remove part of the tumor were cases which the tumor invades important functional areas, the tumors had unclear boundaries. If an attempt is made to remove the entire tumor, it will cause serious neurological deficits, even death.

4.5. Results of multidisciplinary treatment with surgery combined with radiation and chemotherapy

In our study, about 4 weeks after surgery, patients received chemoradiotherapy and then maintained for 6 more cycles of Temozolomide. About the characteristics of radiotherapy, 1/3 of patients received radiation therapy with IMRT/ Vmart technique, applied in tumors located next to critical organs such as brain stem, eye socket to avoid side effects. There were two radiotherapy dose options: 35gy/10Fx in patients in poor condition, low KPS, and 59.4gy/33Fx or 60gy/30Fx in better-fit patients allowing spread radiation. Regarding 3D radiotherapy, the majority of cases included 3 fields. The side effects after chemotherapy and radiotherapy were relatively mild. Fatigue, hair loss and loss of appetite accounted for 66.7%. There were no severe symptoms affecting chemotherapy or radiotherapy.

Evaluation of treatment results: Based on Recist criteria for evaluating solid tumors based on imaging, 7.9% patients had complete response, partial response accounted for 44.7%.

The average progression-free survival time in the patient group was 10.2 ± 1.06 months. Overall survival in the study group was 19.9 ± 1.8 months. According to Thakkar's research from epidemiological reports in the US from 2006-2010, the average overall survival time of patients was 15 months [10], the survival rate after 2 years was 13.7%. According to Patrick Y. Wen (2008), postoperative radiotherapy increased the survival in GBM patients from 3 - 4 months to 7 - 12 months [11]. According to Stupp Roger's study (2005), Temozolomide combine with radiotherapy resulted in improving overall survival to 14.6 months compared to 12.1 months with radiotherapy alone. Resulted from the study, this is a type of brain tumor with high malignancy degree and rapid progression [12]. The combination of multimodality treatment increased survival time and reduces symptoms for patients.

V. CONCLUSION

Glioblastoma was a highly malignant and rapidly progressive. Combination of radiotherapy and chemotherapy after surgery improved symptoms and increase overal survival.

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Original research

CLINICAL AND HISTOPATHOLOGICAL STUDY OF GLOMERULAR DISEASES IN CHILDREN

Tran Kiem Hao[1], Le Thy Phuong Anh[2], Nguyen Thi Thuy Suong[1], Nguyen Huu Son[1], Nguyen Thi Diem Chi[1], Nguyen Dinh Can[1], Hoang Thi Thuy Yen[2]

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ABSTRACT

Objective: *To investigate the histopathological and clinical pattern of glomerular diseases in children.*

Method: *A cross - sectional descriptive study was conducted on 71 children with glomerular disease who underwent kidney biopsy from January 2020 to December 2022.*

Results: *Pure nephrotic syndrome was the main diagnosis before kidney biopsy (59.3%), followed by non - pure nephrotic syndrome with 12.7%, Schonlein Henoch nephritis, Lupus nephritis, IgA nephropathy, accounting for 11.2%, 8.4%, 5.6%, respectively. Hemolytic uremic syndrome and Alport syndrome accounted for 1.4% of each type. After being diagnosed by histopathological results, minimal change disease was most common with 36.6% in the primary group, and Lupus nephritis was found mainly with 15.5% in the secondary group. Among the clinical manifestations of glomerular diseases, hematuria, and extrarenal manifestations were significantly different among the glomerular groups ($p < 0.05$). The ratio of change in diagnosis after the renal biopsy was 38%, in which IgA nephropathy had the lowest ratio, and Lupus nephritis and nephrotic syndrome had the highest ratio.*

Conclusions: *Minimal change disease predominated in the group of primary glomerular disease, and Lupus nephritis was the majority in the group of secondary glomerulonephritis. Hematuria and extrarenal manifestations were clinically significant differences among groups of glomerular diseases.*

Keywords: *Renal biopsy, nephrotic syndrome, histopathology, children.*

I. INTRODUCTION

Glomerular disease is the most common cause of kidney disease in children. Its etiology may be the infectious or non - infectious agents. The most known infectious cause is post - streptococcal glomerulonephritis, followed by other bacteria, viruses, fungi, and parasites. Non - infectious causes are often associated with primary glomerular diseases such as IgA nephropathy, membranous proliferative glomerulonephritis, membranous nephropathy, and systemic diseases such as systemic lupus erythematosus, Henoch - Schönlein [1]. Although systemic diseases may have classic symptoms including butterfly rash, purpura on the skin, arthralgia, and abdominal pain... however, the clinical manifestations of acute glomerular diseases at the onset are quite similar, for example edema, hematuria, and hypertension. Besides, many medical centers are not qualified to do advance medical tests. Therefore, it can be easily misdiagnosed, leading to incomplete treatment, making the disease progress, and possibly leading to end - stage kidney disease.

The glomerular diseases in children are diverse, often requiring long - term treatment, and often recurrence [2]. The treatment response as well as progression to end - stage renal disease depends on the pathological lesions [3]. Knowing well the results of renal histopathology

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will help accurately diagnose the etiology, choose the appropriate therapy as well as predict treatment response. However, only a few medical centers can perform kidney biopsy procedures. To understand the relationship between the clinical pattern and the histopathological characteristics of glomerular diseases in children, we carried out this study to describe the results of the renal histopathology of glomerular diseases in children, and investigate the relationship between the renal histopathology with the clinical pattern of glomerular diseases in children.

II. MATERIALS AND METHODS

A cross - sectional descriptive study was carried out in 71 children with glomerular disease who were indicated for kidney biopsy from January 2020 to December 2022 at Pediatric Center of Hue Central Hospital and Pediatrics Department of Hue University of Medicine and Pharmacy Hospital.

Selection criteria were: Children < 16 years old, diagnosed with glomerular diseases and indicated for kidney biopsy, included: (1) Steroid resistant nephrotic syndrome or steroid dependent nephrotic syndrome in a child > 10 years old, or nephrotic syndrome had manifestations of gross hematuria or renal failure. (2) Acute glomerulonephritis with gross hematuria lasting more than 3 weeks or presenting with acute renal failure lasting more than 2 weeks. (3) Persistent proteinuria nephrotic range for more than 3 months. (4) Lupus nephritis, Scholein Henoch nephritis [2 - 5]

Exclusion criteria were parents or caregivers did not consent to participate in the study.

Clinical investigation included: performing clinical examination, and laboratory tests at the time of kidney biopsy. Collecting variables of age, gender, geography, edema, hypertension, gross hematuria, urine volume, serum albumin, serum creatinine, proteinuria, urinary creatinine, dipstick, and diagnosis before performing renal biopsy.

Renal biopsy was conducted by: an ultrasound - guided percutaneous kidney biopsy with a 16G needle, kidney tissue were sent to read at the Histopathology department, Children's Hospital number 1. Diagnosis which were recorded by histopathological results were collected as a variable.

Data were analyzed by using SPSS software

III. RESULTS

3.1. General characteristics of the research group

There were 71 children with glomerular diseases who were indicated for ultrasound - guided percutaneous kidney biopsy, the average age was 9.1 ± 3.9 years, the group 11 - 15 years old predominated with 42,5%. Male children predominated and the majority of children came from rural areas.

3.2. The diagnosis before biopsy

Table 1: The diagnosis before the biopsy

The diagnosis before biopsy	Frequency (n)	Percent (%)
Henoch Schonlein purpura nephritis (HSPN)	8	11.2
Lupus nephritis (LN)	6	8.4
Pure nephrotic syndrome (pNS)	42	59.3
Nephritic - nephrotic syndrome (NNS)	9	12.7
IgA nephrology (IgA)	4	5.6
Hemolytic uremic syndrome (HUS)	1	1.4
Alport syndrome (Alport)	1	1.4
Total	71	100

Pure nephrotic syndrome was the main diagnosis before renal biopsy (59.3%), followed by nephritis-nephrotic syndrome with 12.7%, Schonlein Henoch nephritis, Lupus nephritis, IgA nephropathy, accounting for 11.2%, 8.4%, and 5.6%, respectively. Hemolytic uremic anemia and Alport syndrome accounted for 1.4% of each type.

3.3. Histopathological results

Table 2: Histopathological results of glomerular diseases

Group	Histopathological results	Frequency (n)	Percent (%)
Secondary glomerular disease	Henoch Schonlein purpura nephritis (HSPN)	6	8.5
	Lupus nephritis (LN)	11	15.5
	Secondary focal segmental glomerulosclerosis (sFSGS)	1	1.4
Primary glomerular disease	Minimal change disease (MCD)	26	36.6
	Primary Focal segmental glomerulosclerosis (pFSGS)	19	26.8
	IgA nephrology (IgA)	6	8.5
	Membranoproliferative glomerulonephritis (MPGN)	1	1.4
	Membranous nephropathy (MN)	1	1.4
Total		71	100

The group with primary glomerular disease (74.6%) accounted for the majority comparing with the group with secondary glomerular disease (25.4%). In the primary group, minimal change disease was the most common with 36.6%, in the secondary group, Lupus nephritis was found mainly (15.5%).

3.4. Clinical features of glomerular diseases

Table 3: Clinical features of glomerular diseases

Clinical features	Hypertension		Gross hematuria		Oliguria		Extrarenal manifestations	
Causes	Frequency (n)	Percent %	Frequency (n)	Percent %	Frequency (n)	Percent %	Frequency (n)	Percent %
HSP (n=6)	1	16.7	3	50	0	0	6	100
LN (n=11)	6	54.5	5	45.5	2	18.2	4	36.4
sFSGS (n=1)	0	0	1	100	0	0	0	0
MCD (n=26)	3	11.5	0	0	2	7.7	0	0
pFSGS (n=19)	5	26.3	1	5.3	1	5.3	0	0
IgA (n=6)	0	0	5	83.3	0	0	0	0
MPGN (n=1)	1	100	0	0	0	0	0	0
MN (n=1)	0	0	1	100	0	0	0	0
Total (n=71)	16	22.6	16	22.6	5	7.0	10	14.1
p	> 0,05		< 0,05		> 0,05		< 0,05	

In the clinical manifestations of glomerular disease groups, hematuria symptom, and extrarenal manifestations were significantly different between groups of glomerular diseases ($p < 0.05$).

3.5. The rate of the change in diagnosis before and after kidney biopsy

Table 4: The rate of the change in diagnosis before and after kidney biopsy

		Pre - biopsy diagnosis							Total
		HSPN	LN	pNS	NNS	IgA	HUS	Alport	
Post - biopsy diagnosis	HSPN	6	0	0	0	0	0	0	6
	LN	2	5	0	3	0	1	0	11
	MCD	0	0	25	1	0	0	0	26
	pFSGS	0	1	13	4	0	0	1	19
	IgA	0	0	2	0	4	0	0	6
	MPGN	0	0	0	1	0	0	0	1
	MN	0	0	1	0	0	0	0	1
	sFSGS	0	0	1	0	0	0	0	1
Total		8	6	42	9	4	0	1	71

Table 5: The rate of change in diagnosis after renal biopsy

Change in diagnosis	Frequency (n)	Percent (%)
Yes	27	38.0
No	44	62.0
Total	71	100

The rate of change in diagnosis after kidney biopsy was 38%.

IV. DISCUSSION

In Table 1, our study noted that pure nephrotic syndrome was the main diagnosis before kidney biopsy (59.3%), followed by nephritic-nephrotic syndrome with 12.7%, Schonlein Henoch purpura nephritis, Lupus nephritis, IgA nephropathy, accounting for 11.2%, 8.4%, and 5.6%, respectively. Hemolytic uremic anemia and Alport syndrome accounted for 1.4% of each type.

Nguyen Thi Hong Duc's study recorded that pre-biopsy diagnosis were nephrotic syndrome with 46.9%, acute glomerulonephritis with 15.6%, Lupus nephritis with 21.9%, recurrent hematuria with 12.5 %, renal failure of unknown cause with 3.1% [6].

Lee SA's study in 318 cases showed that pre-biopsy clinical diagnosis included 114 patients (35.9%) with asymptomatic urine abnormalities, 44 patients (13.9%) with isolated hematuria, 70 patients (22.0%) hematuria with proteinuria; 93 patients (29.3%) with nephrotic syndrome; 57 patients (18.0%) with acute glomerulonephritis; 38 patients (11.9%) had Henoch Schönlein purpura nephritis; 4 patients (1.2%) with Lupus nephritis; and 12 patients (3.7%) had other diseases, such as acute renal failure, Alport syndrome, hemolytic uremic syndrome…[7]

Thus, the clinical diagnosis of glomerular diseases before renal biopsy is also quite diverse. Among them, nephrotic syndrome is still one of the most common diagnosis.

Regarding the histopathological results of the glomerular group listed in Table 2, we found that primary glomerulonephritis (74.6%) accounted for the majority comparing with the secondary glomerular group (25.4%). In the primary glomerulonephritis, minimal change disease was the most common with 36.6%, in the secondary glomerulonephritis, Lupus nephritis was found mainly (15.5%).

Research by Huynh Thoai Loan from 2008 to 2010 in 262 children showed that the rate of minimal change disease was 24.05%, Lupus nephritis was 23.66%, focal segmental glomerulosclerosis

was 17.94%, IgA nephrology was 11.45%, Henoch schonlein purpura nephritis was 3.44%, membranoproliferative glomerulonephritis was 1.53%, and membranous nephrology was 1.53% [8].

A group of Korean researchers published the results of kidney biopsies in 318 children over 27 years as follows: IgA nephropathy was the most common at 27.9%, followed by minimal change disease at 21.3%, membranoproliferative glomerulonephritis 7.2%, and focal segmental glomerulosclerosis 3.4%. In the group of secondary glomerulonephritis, Schonlein Henoch nephritis accounted for 12.2% while Lupus nephritis accounted for 1.5% [7].

A 16 - year Morroco study in 112 children showed that primary nephropathy accounted for 59.8% of cases, with minimal change disease predominating in 40.2% of cases. Secondary nephropathy accounted for 27.7% of cases, with mainly Lupus nephritis (11.6%), followed by Henoch-Schonlein purpura nephritis (6.2%) and post-infectious glomerulonephritis (3.6%). There was one case of hepatitis B virus-associated membranous nephritis. Chronic glomerulonephritis accounted for 12.5% of cases [9].

These results may be explained by the difference of racial characteristics, regions and medical conditions, however, in general, primary glomerulopathy was the predominant group of glomerular diseases, and minimal change disease was the most common histopathological finding.

When learning about the clinical pattern of glomerular diseases in children, we noted that the overall prevalence of hypertension in the study group was 22.6%. There was no difference in hypertension among glomerular diseases ($p > 0.05$). In the study of Nguyen Thi Hong Duc, the rate of hypertension in renal biopsy patients was 31.3% [6]. Regarding the group of primary glomerular diseases, mainly nephrotic syndrome, we found in Phan Ngoc Hai's study the rate of hypertension was 13.9% [10], and 10.8% of children in Nguyen Van Sang's study showed signs of hypertension [11]. This result was quite similar to our study. In Thai Thien Nam's study on Lupus nephritis in children, the rate of hypertension accounted for 50% [12]. Hypertension is a common symptom of glomerular diseases. Hypertension is result from glomerular damage as well as extraglomerular mechanisms. Renal factors such as hypoalbuminemia lead to a decrease in oncotic pressure, a decrease in glomerular filtration rate, an activation the Renin - Angiotensin - Aldosteron system, which causes salt and water retention, vasoconstriction, and increases blood pressure; or fibrotic lesions in the glomeruli also contribute to hypertension [13, 14]. Recently, the feedback reaction between albuminuria and the glomerular loops has also contributed to hypertension [14]. Extrarenal mechanisms include the use of drugs (corticosteroids, cyclosporine A), genetic factors, diet, and atherosclerotic factors [13]. Therefore, symptoms of hypertension are not specific to any group of glomerular diseases.

In the group of primary glomerular disease, the majority of patients did not have gross hematuria. In the group of secondary glomerular disease, the rate of gross hematuria was higher. There was a significant difference in hematuria among groups of glomerular disease ($p < 0.05$). In clinical evaluation, physician based on gross hematuria to access the cause of primary nephrotic syndrome. Nephrotic syndrome without glomerulonephritis is mostly idiopathic nephrotic syndrome such as minimal change disease, and focal segmental glomerulosclerosis. Nephrotic syndrome with glomerulonephritis hematuria is common in membranous glomerulopathy, membranous proliferative glomerulonephritis, IgA nephropathy… [15]. Therefore, gross hematuria is a valuable symptom to help identify the etiology of glomerular diseases.

The majority of patients did not have oliguria, or anuria (table 3). The results of our study were lower than that of Nguyen Thi Hong Duc with 21.9% of patients with oliguria [6].

Extrarenal manifestations were the majority in the secondary pathology group, while the primary glomerular disease group had no extrarenal manifestations. Notably, 7 of 11 patients with Lupus nephritis had no extrarenal manifestations, which easily led to the omission of diagnosis in centers that were not able to do advance medical tests.

Assessing the rate of diagnostic change before and after the kidney biopsy, we found in Table 4 that the diagnosis of pure nephrotic syndrome was changed

the most after kidney biopsy, and IgA nephropathy had a 100% concordance rate between clinical diagnosis and post - biopsy diagnosis. The overall rate of change in diagnosis post - biopsy was 38%.

According to research by Huynh Thoai Loan and Tran Thi Kim Anh, the diagnosis of nephrotic syndrome and Lupus nephritis were the two pre-biopsy diagnosis that changed the most [8, 16]. The rate of Tran Thi Kim Anh's study was 10% [16]. According to the study of Pilania, the diagnosis after biopsy was changed at 47% [17]. This ratio varied between the diagnostic orientation, the laboratory centers, and the experience of doctors. However, renal biopsy and histopathology have shown an important role in the definitive diagnosis of glomerular diseases, thereby providing the basis for selecting the best treatment methods for the patient.

V. CONCLUSIONS

In children with glomerular diseases, minimal change disease was most common in the primary group, Lupus nephritis was seen mainly in the secondary group. Hematuria and extrarenal manifestations were clinically significant differences among glomerular diseases. The rate of change in diagnosis after renal biopsy was 38%, in which IgA nephropathy had the lowest ratio, Lupus nephritis and nephrotic syndrome had the highest ratio.

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Original research

BACTERIAL CONTAMINATION IN THE OPERATING ROOM AT HUE CENTRAL HOSPITAL, 2nd BRANCH

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ABSTRACT

Objectives: *This study aims to evaluate the microbial contamination level and identify bacterial colonization of the operating room in the hospital.*

Methods: *Three sampling procedures were used in this study, which includes swabbing, air sampler and contact agar plate. Collected samples from 8 ORs were transported and microbiologically processed using standard procedures. Bacteria were identified by morphological, biochemical tests and Vitek 2 Compact system. Microbiological criteria were based on recommendation of the Ministry of Health.*

Results: *The incidence of positive cultures was 285/600 (47.50%). The most common isolates were Gram - positive bacteria (98.25%) while low rate of Gram - negative bacteria (1.75%) was surveyed with Pseudomonas sp. (0.7%) and Enterobacter cloacae (1.05%). The water used for surgical hand washing illustrated the existence of Staphylococcus blanc (60%) and each of Pseudomonas sp. and Enterobacter cloacae (20%). Air contamination were observed with Bacillus sp. (46.90%) and Staphylococcus blanc (53.10%). Environmental surfaces were detected 7 species, of which 4 threaten strains including Staphylococcus aureus accounted for 5.55%, followed by Streptococcus β - hemolytic (0.79%), Pseudomonas sp. (0.79%) and Enterobacter cloacae (1.59%). Surgeons's hand samples were isolated with Bacillus sp. (14.55%) and Staphylococcus blanc (1.81%). The rate samples of ORs surfaces reaching level A and B accounted for 91.49% and 8.51% while none of the samples approach level C and level D. The rate of qualified samples in terms of air, water for surgical hand washing, surfaces of medical instruments and surgeons' hands was remarkably high with 87.59%, 98.44%, 95.24% and 100%, respectively.*

Conclusion: *Our study showed various bacteria isolated, of which pathogenic species occupied very low percentage. Especially, the rate of samples in the study that meet microbiological standards was remarkably high according to Ministry of Health recommendation.*

Keywords: *Operating rooms (ORs), surgical hand washing (SHW), surgical site infection (SSI), colony forming unit (CFU), brain heart infusion broth (BHI).*

I. BACKGROUND

Surgical site infection (SSI) has become a major issue that triggers to patient morbidity and death [1, 2]. A study reported that the annual cases of healthcare - accquired SSI was estimated to be 2 million in America, leading to increasing length of hospital stays with 7.4 days and incurred cost with 130 million USD [2]. Other study showed that 5% - 10% of approximetly 2 million patients undergoing surgery suffered from SSI in Vietnam [1, 2]. This gives rise to twofold increase in the length of hospital stays and treatment costs [1, 3]. The controlled environment of ORs remains potentially risky for patient due to a number of factors such as ventilating system, cleaning, sterilization, patients transportation, medical equipments, waste of injuries and water source for hand hygiene, which are able to be associated with microbial growth

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conditions [4 - 6]. This present study would reveal findings of the microbial prevalence as well as the microbial contamination level related to air, surface, water and identify bacterial colonization at 8 ORs in Hue Central Hospital 2nd Branch.

II. MATERIALS AND METHODS

The study was conducted at Hue Central Hospital and Hue Central Hospital, 2nd Branch from January 2020 to September 2021. The permission for the study was taken from Director Board of Hue Central Hospital. All samples were collected before surgical performances.

2.1. Air samping and analysis

Air sampling was implemented via an active air sampler of Germany MERCK - KGA MAS 100 brand which collects a predetermined volume of air with 1m3 in 10 minutes and capture the microorganism onto agar - based growth medium such as Blood agar, MacConkey agar, Nutrient agar. These were then transported to microbiological laboratory and incubated at 37°C in 18 - 24 hours under aerobic conditions [7]. After incubation, the quantity of colonies on Nutrient agar plates were counted as the results of total aerobic bacteria per $1m^3$ (CFU/m^3) and isolates were identified by colony characteristics, gram stain and standard biochemical test as well as Vitek 2 Compact system. Air standard in ORs is recommended by Ministry of Health given below [3, 8, 9]:

- An empty theatre bio load should not exceed $35CFU/m^3$
- During surgery bio load should not exceed $180CFU/m^3$
- None of harmful bacteria are present in operation theatres

2.2. Surfaces sampling and analysis

Sterile swabs moistened in sterile distilled water and rolled over the surfaces of medical equipments and surgeons' hands. All collected swabs were then immediatetly put into test tubes of BHI (brain heart infusion broth) which is a liquid medium used for the enrichment of microorganisims growth. These were then transported to microbiological laboratory and incubated at 37°C for 18 - 24 hours under aerobic conditions. After incubation, BHI tubes with good turbidity were chosen to inoculate on agar plates. The plates, afterwards, were continued to be put into the incubator and set the conditions as the previous step. After 18 - 24 cultivation, isolates eventually were identified by colony characteristics, gram stain, standard biochemical test and Vitek 2 Compact system [8, 9].

Contact - plate sampling is the method making the bacterial load on surfaces visible. Nutrient agar plates were used to press against the surfaces such as walls and floors for a short moment in 10s. These were then transported to microbiological laboratory and incubated at 37°C for 18 - 24 hours under aerobic conditions. After incubation, the quantity of colonies on the plates was counted as the results of total aerobic bacteria per $25cm^2$ ($CFU/25cm^2$). The surface standard in ORs is recommended by Ministry of Health given below [3, 8, 10]:

- Level A: < 1 $CFU/25cm^2$, Level B: < 5 $CFU/25cm^2$, Level C: < 25 $CFU/25cm^2$, Level D: < 50 $CFU/25cm^2$
- None of harmful bacteria are present in operation theatres.

2.3. Water sampling and analysis

In order to take water samples for surgical hand washing, faucets, firstly, were heated to pre-disinfect and flushed for about 3 - 5 minutes. Test tubes containing 10ml BHI were used to take water samples and then transported to microbiological laboratory and incubated at 37°C for 18 - 24 hours under aerobic conditions. After incubation, BHI tubes with good turbidity were chosen to inoculate on agar plates. The plates, afterwards, were continued to be put into the incubator and set the conditions as the previous step. After 18 - 24 cultivation, isolates eventually were identified by colony characteristics, gram stain, standard biochemical test and Vitek 2 Compact system [8]. The standard of water for SHW in ORs is recommended by Ministry of Health given below [11, 12]: None of bacteria are present in water for surgical hand washing.

III. RESULTS

600 samples were collected from air, water for SHW, surfaces including medical equipments, walls and floors, of which 285 (47.50%) cultures were positive (Figure 1). The most common isolates were Gram - positive bacteria with 98.25% while Gram - negative bacteria occupied only 1.75% (Figure 2).

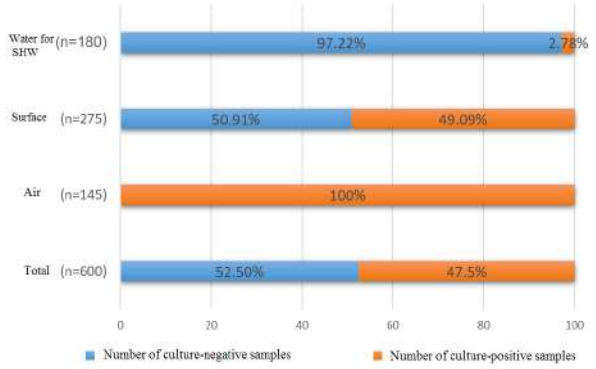

Figure 1: Percentage of positive and negative samples

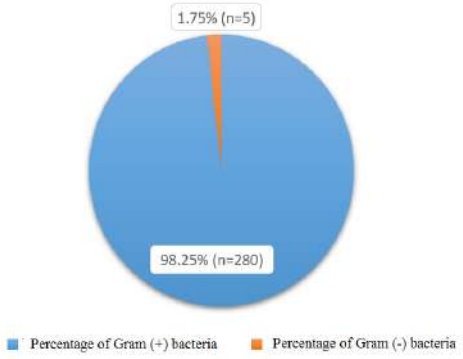

Figure 2: Percentage of Gram - positive and Gram - negative

7 bacterial species were identified in different ORs including *Bacillus sp.* accounted for 48.42% bacteria isolated, followed by *Staphylococcus blanc* (46.32%), *Staphylococcus non - coagulase* (2.46%), *Staphylococcus aureus* (0.70%), *Streptococcus β - hemolytic* (0.35%), *Pseudomonas sp.* (0.70%) and *Enterobacter cloacae* (1.05%) (Figure 3).

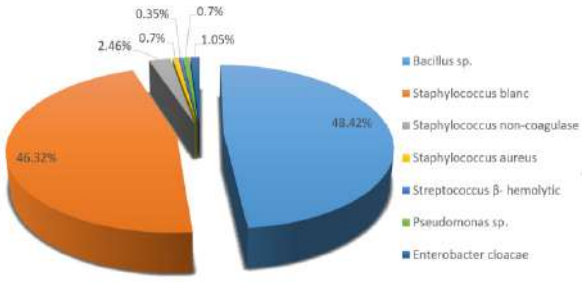

Figure 3: Types of bacteria identified from ORs

Figures 4 showed a predominance of *Bacillus sp.* and *S. blanc* which are less likely to cause diseases among 8 ORs. *Staphylococcus non - coagulase* was observed in OR1, OR3 and OR4 with 5.26%, 5.41% and 9.09% of bacteria isolates, respectively. The percentage of pathogenic bacteria was very low. *S.aureus* was only present in the OR1 with 5.26%. *Streptococcus β - hemolytic* was detected in the OR3 with 2.70%. *Pseudomonas sp.* occupied 3.03% bacteria isolated in the OR3 and 2.63% was the rate of *Enterobacter cloacae* found in OR1.

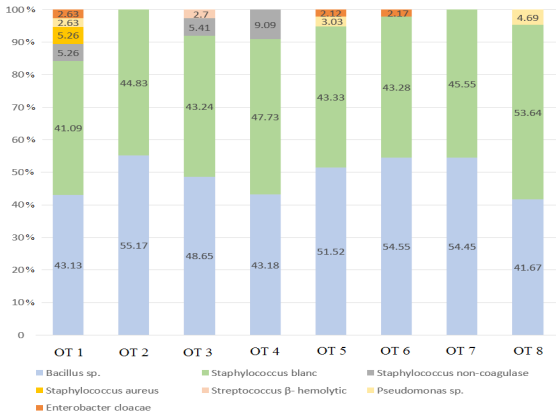

Figure 4: Types of bacteria from different ORs

Figure 5 reveals that the quantity of air samples containing over 35 CFU/m^3 was 18 (12%), of which OR1 and OR2 accounted for 6.25% positive cultures which touched the lowest rate while OR3 and OR4 accounted for 16.67% reaching the top rate compared to the others ORs. Bacteria isolated from environmental

air given in Figure 6 such as *Bacillus sp.* and *S. blanc* were not involved in the group of pathogenic species according to the Ministry of Health recommendation.

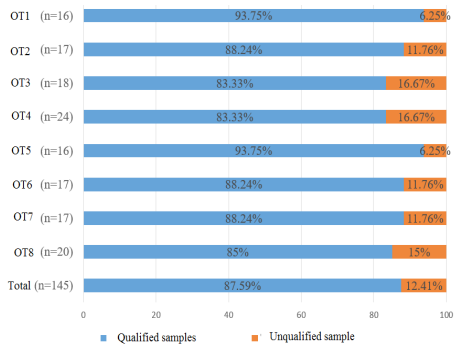

Figure 5: Microbial air contamination level

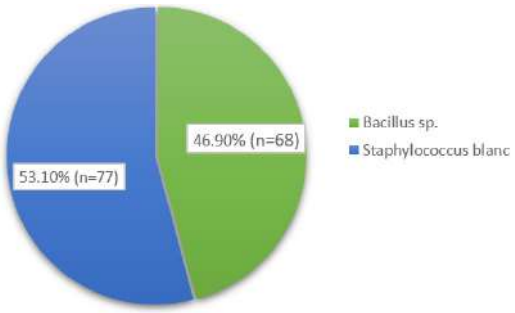

Figure 6: Types of bacteria identified from air samples

7 types of bacteria were surveyed among the medical equipments in the ORs. *Bacillus sp.* and *S. blanc* occupied 49.21% and 40.48%, followed by *Staphylococcus non - coagulase* (5.55%), *S. aureus* (1.59%), *Enterobacter cloacae* (1.59%) and each of *Streptococcus β - hemolytic* and *Pseudomonas sp.* (0.79%) (Figure 7).

Figure 8 showed that 46/55 samples taken from surgeon hands gave negative results with 83.64% and there was the presence of *Bacillus sp.* (14.55%) and *S. blanc* (1.81%) which are not involved in the group of pathogenic bateria.

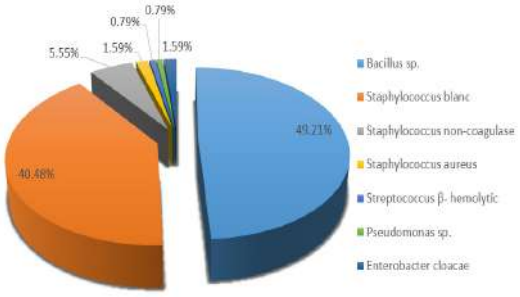

Figure 7: Medical equipments'surface contamination

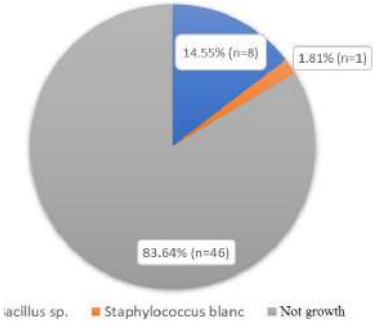

Figure 8: Surgeon hand's surface contamination

Figure 9 illustrates that none of surface cultures among 94 samples collected reach level C (< 25 CFU/25m^2) and level D (< 50 CFU/25cm^2) according to the Ministry of Health standard for classification of operation room cleanliness [3, 13].

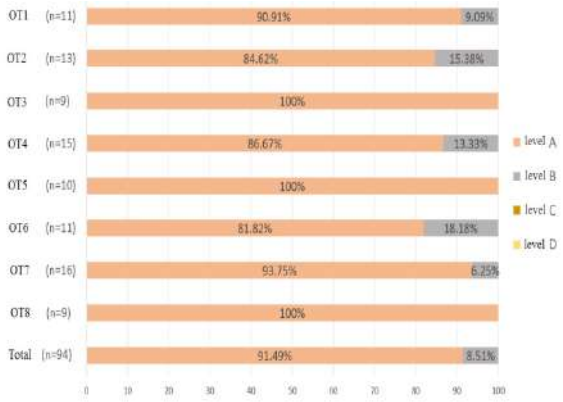

Figure 9: ORs's surface (floor & wall) contamination level

182 samples of water for SHW were collected, of which only 1.11% positive cultures result in the presence of *Enterobacter cloacae* (20%) and *Pseudomonas sp.* (20%) (Figure 10 & 11).

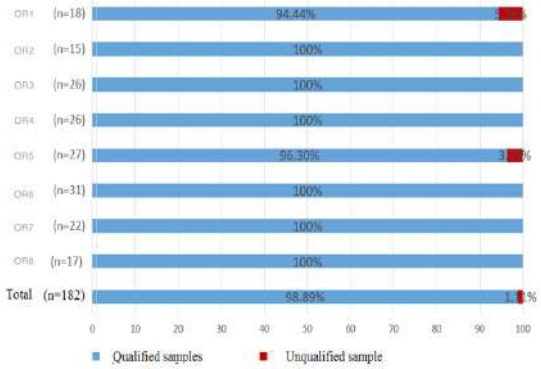

Figure 10: Water for SHW contamination level

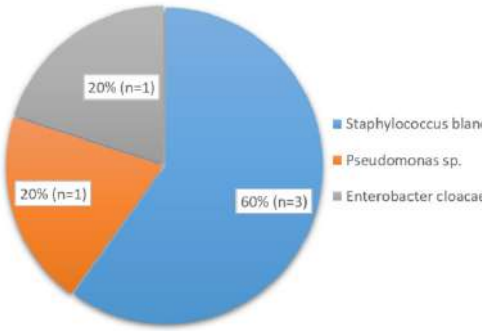

Figure 11: Types of bacteria identified from water for SHW

IV. DISCUSSION

A number of studies showed various results in the rate of positive cultures. Kausar et al (2020) reported that the positive rates occupied 72.82% [14]. Additionally, 48.3% and 24.7% were also the proportion of the positive ones according to Baban et al (2019) and Laham et al (2011), respectively [15, 16].

It is obvious that *Bacillus sp.* and *Staphylococcus blanc* were the most common isolated from the ORs. The rate of *Bacillus sp.* isolated in a number of studies was fewer than those in this study. To illustrate, *Bacillus sp.* seized 26.17% reported by Kausar et al (2020) [14] and 26.67% according to Bekkari H et al (2016) [17]. *Staphylococcus non-coagulase* is considered as an exogenous organism that can be normal skin flora of medical personnel and patient. One of the most dangerous bacteria isolated in the study was S. aureus that its isolates rate was much fewer than those in other studies such as Kausar et al (2020) [14] with 15.1% and Baban et al (2019) with 52% [16]. Besides, despite the existence of a number of dangerous strains like *Streptococcus β - hemolytic, Pseudomonas sp.*, their proportion was still extremetly low with 0.35%, 0.70% and 1.50%, respectively.

A study of Raksha et al (2019) found various species such as *Staphylococcus non - coagulase, E.coli, Streptococcus.sp, S. aureus* and *Micrococci* [18]. A report from Bekkari et al (2016) showed the presence of *Pseudomonas vesicularis* and *Streptococcus.sp* isolated in the environment of ORs [17]. Three species detected in the study of S. Ensayef (2009) were *Staphylococcus epidermidis*, *S.aureus* and *Pseudomonas aeruginosa* [19]. Nahed A. Al Laham et al (2011) gave information about 6 types of bacteria in the studied ORs including *Enterobacter, E.coli, Klebsiella, Acinetobacter, Pseudomonas and Streptococcus* [15].

The environmental hygiene and air treatment in the studied ORs was very good with none of pathogenic strains isolated and 87.59% air sample meets the microbiological standard.

S.aureus, Streptococcus β - hemolytic, Pseudomonas sp., Enterobacter cloacae were 4 species that fail to the meet the standard of microbiological surfaces in the ORs. *S.aureus* was detected in an anaesthetic face mask in OR1. In spite of low rate of *S.aureus* (1.59%) isolated, it must be concerned due to the risk of infection relating to skin, blood… as well as strong antibiotic resistance [20]. *Streptococcus β - hemolytic* (0.79%) was appeared on the surface of a medical equipment trolley in OR3. *Pseudomonas sp.* (0.79%) was found in a control button of electric scaple and *Enterobacter cloacae* (1.59%) was present on a surgical lighting in OR6.

It is noticeable that 91.49% cultures approached level A while the others were belong to level B with 8.51%. Particularly, 100% samples collected from OR3, OR5 and OR8 reached level A. It is amitted that environmental sanitation in the ORs of Hue Central Hospital - 2nd branch was very good. In our results, relatively clean sites were floors and walls of all ORs.

The result reflected that the surgical hand washing practice of surgeons in the studied ORs was very good with the high rate of negative cultures. As for

the positive ones, the bacterial isolates like *Bacillus sp.* and *S. blanc* are less likely to cause diseases and easily eliminated by routine hand hygiene.

Although the rate of positive samples of water was extremely low, it must be concerned that the two species *Enterobacter cloacae* and *Pseudomonas sp.* are found widely in the environment and fairy common pathogens involved in infections aquired in a hospital setting.

V. CONCLUSION

Microbial quality of air, surface and water in ORs might be considered as a mirror reflecting hygienic conditions of health - care facilities. Our study showed various bacteria isolated, of which pathogenic species occupied very low percentage. Especially, the rate of cultures in the research that meet the microbiological standards was remarkably high according to Ministry of Health recommendation.

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Original research

OUTCOMES OF TOURNIQUET - LESS TOTAL KNEE ARTHROPLASTY

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ABSTRACT

Introduction: *Tourniquet use in total knee arthroplasty (TKA) provides a bloodless field to improve visualization; however, the arguments for improving cement fixation, decreasing operative time, and decreasing overall blood loss have not been supported by the literature. Tourniquetless TKA is gaining popularity with the reported less postoperative pain and improved knee function in addition to no evident increased risk compared to tourniquet use. This study assessed the outcomes of tourniquetless TKA surgery in Hue Central Hospital.*

Methods: *35 patients with end - stage knee osteoarthritis undergoing tourniquetless TKA surgery were included in this study. Demographic data, physical examination, and radiographic parameters were collected pre - and post-operatively. Intra - and postoperative complications were also reported. The patient's knee function and clinical outcomes were reassessed at the 1 - month and 3 - month follow - up times.*

Results: *Tourniquetless TKA showed significant improvements regarding knee pain, knee alignment, and knee function. No significant complications were reported post - operatively.*

Conclusion: *Tourniquetless TKA can be safely performed on a routine basis on end - stage knee osteoarthritis patients with relatively no significant complications.*

Keywords: *Total knee arthroplasty, tourniquet, mechanical alignment, KOOS, knee osteoarthritis.*

I. INTRODUCTION

It has been a widely used practice to utilize a tourniquet during total knee arthroplasty (TKA). There were proposed advantages of providing better visualization, reducing intraoperative blood loss, improving cement fixation, and decreasing operation time [1 - 3]. However, significant hazards associated with the use of tourniquets have been brought to attention, such as venous ischemia, amplified pain, venous thromboembolisms, nerve impairment, and infection [4 - 6]. There is a trend of performing TKA surgeries without the use of tourniquets in the orthopedic society. At the poll regarding current practice patterns conducted at the 2020 Annual Meeting of the American Association of Hip and Knee Surgeons (AAHKS), tourniquets were used by 24% of surgeons in all cases, a decrease from 37% in 2009, while 47% used them in all cases except those involving vascular concerns. 16% of surgeons only used tourniquets during exposure and cementation (compared to 5% in 2009), and 13% chose not to use them at all [7]. There were multiple studies demonstrating the benefits of tourniquetless TKA including avoiding tourniquet-specific complications [6, 8], decreased postoperative pain [9, 10], reduced analgesic use [9, 11], less swelling [10], improved postoperative knee range of motion and function [11 - 13], and enhanced outcome scores [11, 14]. Despite still being controversial, tourniquetless TKA has been gaining momentum in the literature challenging the conventional use of tourniquets in TKA procedures. At our national orthopedic center, we have been consistently utilizing the tourniquetless TKA technique since 2018 with a committed process of the entire surgical team. Our study was to assess

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the outcomes of tourniquetless TKA surgery at Hue Central Hospital, Vietnam.

II. MATERIALS AND METHODS

35 patients with Kellgren Lawrence stage 4 [15] knee osteoarthritis who were admitted to our orthopedic center from December 2021 to February 2023 were included in this study. All the patients underwent medical history inquiry, clinical examination, radiographic investigation, and elective tourniquetless total knee arthroplasty surgery by two senior orthopedic surgeons. The standard medial parapatellar approach and mechanical alignment technique were used in all TKA surgeries. Tourniquets were not used at all, in addition, 1 gram of intravenous tranexamic acid was administered pre - operatively. Deep venous thrombosis prophylaxis started 12 hours post-operatively. A consistent protocol, as recommended by Stronach et al [5], was followed in all TKA procedures, as detailed in Table 1. We also recorded demographic data, pre - and post - operative Knee Injury and Osteoarthritis Outcome Score (KOOS) [16], and other research variables including time of operation, intra - operative blood loss, hospital stays, complications and KOOS score at 1 - month and 3 - month follow up for data analysis. Statistical analysis was performed using IBM® SPSS® software version 25.0. The study garnered approval from the Institutional Review Board (IRB) of Hue Central Hospital, which served as the primary location for all research - related activities.

Table 1: Recommended Techniques for Tourniquetless TKA

• Screen for and correct preoperative anemia
• Give tranexamic acid in perioperative setting (oral, IV, and/or local administration)
• Do not apply tourniquet to the extremity
• Have a sterile tourniquet available if needed
• Preemptive analgesia and multimodal pain control are recommended
• Hypotensive anesthesia (mean arterial pressure of 60) helps minimize intraoperative blood loss
• Keep the knee flexed for most of the procedure
• Coagulate the genicular arteries on joint entry
• Complete hemostasis of all small bleeding vessels is not necessary
• Place anterior chamfer fragment in femoral canal as bone plug (if intramedullary guide used)
• Multimodal periarticular injection used to assist in hemostasis
• Prepare bone for cementation in deep flexion
• Thoroughly irrigate all exposed bone surfaces to remove lipid marrow
• Use a laparatomy sponge and suction all bone surfaces to clean before cementation
• Place cement on implant and bone surfaces
• Cement tibia first followed by femur and patella
• Continue to keep all interfaces dry before implants are placed
• Once components are implanted, avoid motion of the knee during cementation
• Allow cement to cure with knee in extension

III. RESULTS

Of the 35 patients included in the study, there were 9 males (25.7%) and 26 females (74.3%), with a mean age of 63 ± 9.7 and mean body mass index (BMI) of 24.3 ± 2.7. Regarding radiographic alignment, neutral alignment was defined as 0 ± 3°, while mild valgus/varus was defined as 3 - 6° and severe valgus/varus was defined as > 6°. All TKA surgeries utilized mechanical alignment technique. Table 2 shows the results of preoperative and postoperative numbers of patients and their respective knee alignments.

Table 2: Radiographic alignment pre - and post - operatively

	Severe valgus N (%)	**Mild valgus N (%)**	**Neutral N (%)**	**Mild varus N (%)**	**Severe varus N (%)**
Pre - Op	2 (5.7%)	7 (20.0%)	11 (31.4%)	15 (28.6%)	5 (14.3%)
Post - Op	0 (0%)	1 (2.8%)	29 (82.9%)	5 (14.3%)	0 (%)

In our study, regarding clinical outcomes of patients who underwent tourniquetless TKA surgery, the mean time of operation was 101 ± 17.2 minutes, with an intra - operative blood loss estimation of 360 ± 211ml and hospital stays averaging 5 ± 1.1 days. No major complications and no infections were recorded at

the time of discharge and 3 - month follow up. There was one patient with non - displaced longitudinal tibial fracture after a falling at home, who was then admitted to the hospital and treated with cast immobilization.

With respect to KOOS Score, significant improvements were observed over time, specifically from pre-op to discharge, as well as the 1 - month and 3 - month follow up assessments. Table 3 presents the normalized score for the 5 subscales of KOOS Score at four distinct time points.

Table 3: KOOS normalized score over time

	Pre - op	**Discharge**	**1 - month**	**3 - month**
Pain	41	82	89	93
Symptom	60	82	90	94
ADL	58	82	86	89
Sport/Rec	15	22	21	22
QoL	23	81	80	85

IV. DISCUSSION

In this study, we conducted the tourniquetless TKA surgeries for end-stage osteoarthritis patients and evaluated the short outcomes of the techniques. Our sample's baseline characteristics closely resembled those in previous studies conducted by Alexandersson et al [17] and Ejaz et al [11], including parameters such as sample size, mean age, and BMI. However, it is worth noting that the gender distribution in our study was notably skewed, with nearly 3 females to 1 male. This pattern resembles the predominant numbers of female in the article by Miyamoto et al [18].

In the realm of knee alignment principles and surgical techniques, there exist three primary categories [19]. The traditional Systematic Alignment, incorporates techniques such as mechanical alignment [20 - 22], with the primary objective of Systematic Alignment is the restoration of the knee's neutral alignment, irrespective of any preoperative deformities. In contrast, the Patient - Specific Alignment, includes approaches like Kinematic Alignment [23], which seeks to preserve the patient's native alignment and joint line inclination. Finally, the Hybrid Alignment, encompasses a variety of methods such as adjusted mechanical alignment [24, 25], restricted kinematic alignment [26], inverse kinematic alignment [25, 27], and functional alignment. Within this category, the target alignment is set at $180^{o} \pm 3^{o}$ [19]. These distinct categories provide a comprehensive framework for addressing alignment issues in knee surgery, however, they remain subjects of controversy, with a lack of consensus on which alignment provides best results. In our study, we implemented the traditional mechanical alignment as our sole technique with the standard medial parapatellar approach. All our patients achieved postoperative knee alignment within the range of neutral or mild varus/valgus, with 82.9% achieving neutral alignment, and 14.3% and 1.8% displaying mild varus and mild valgus, respectively. There is substantial agreement among authors that a slight under-correction of preoperative varus deformity knees can yield comparable or even superior outcomes compared to neutral alignment [24, 28, 29]. While not as widely reported as varus alignment, there have been articles to suggest a slight under-correction in preoperative valgus knees can result in similar outcomes compared to those achieved with neutral alignment [30, 31].

Mean operating time of our study was 101 ± 17.2 minutes, slightly longer than previous studies by Ledin et al [32], Aglietti et al [2], Ayik et al [33], but the difference was not significant. Intra-operative blood loss in our study was similar to several previous studies by Dong et al [34], Tai et al [35], and significantly lesser than Goel et al [36], Pfitzner et al [37], however, the difference of blood loss was largely altered by the method of calculation employed by authors. Length of hospital stay in our study was also similar to the study by Huang et al [10], with 5 ± 1.1 and 5.12 ± 0.4 days, respectively. The above clinical parameters were frequently

evaluated by studies comparing outcomes between tourniquet and non-tourniquet TKA surgeries. A systematic review and meta-analysis conducted by Ahmed et al demonstrated that there was no differences in overall blood loss between TKA surgeries with and without tourniquet. Tourniquet TKA surgeries was associated with a shorter duration of surgery but a longer hospital stay compared to tourniquetless surgeries [38]. The debate regarding the use of tourniquet in TKA procedures keeps going hot in literature, there is a trend of surgeons transition away from a tourniquet in their TKA surgeries. Recommendations for a process aimed at optimizing the benefits and minimizing the drawbacks of tourniquetless TKA procedures was also reported and put into practice [5].

When assessing tourniquetless TKA outcomes with the KOOS score, our findings indicated notable improvements from the pre-operative stage to discharge, with scores consistently progressing positively during the 1-month to 3-month follow-up period. These findings are in accordance with Ejaz et al [11], who found that not only significant advancements were achieved in early stage of postoperative but also these enhancements were superior when compared to the group that used tourniquet during surgery. No major complications or infections were reported during our study period, nevertheless, for a more comprehensive assessment of potential complications, a longer follow-up duration should be considered.

V. CONCLUSION

Tourniquetless TKA can be safely performed on a routine basis on end-stage knee osteoarthritis patients with relatively no significant complications.

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Original research

RED BLOOD CELL - PLATELET RATIO (RPR) AND HEMOGLOBIN - PLATELET RATIO (HPR) IN PATIENTS WITH RHEUMATOID ARTHRITIS: A STUDY AT HUE UNIVERSITY OF MEDICINE AND PHARMACY HOSPITAL

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ABSTRACT

Background: *Rheumatoid arthritis (RA) is an autoimmune disease that causes chronic inflammation of the joints, resulting in destruction and deformation of bones and cartilage. In addition to causing joint damage, up to 30 - 70% of RA patients have chronic anemia that reduces quality of life. The inflammatory process affects some red blood cell and platelet indices such as increased platelet count, anemia and hypochromic microcytic cells. Red blood cell - platelet ratio (RPR) and hemoglobin - platelet ratio (HPR) are considered as indicators to help assess inflammation and activity level in patients with RA. This study describes hematological characteristics and the relationship of RPR and HPR indices with inflammation in patients with RA.*

Methods: *The study was conducted on 30 patients with RA at the Department of General Internal Medicine - Endocrinology - Musculoskeletal and a control group of 30 healthy people who came to hospital of Hue University of Medicine and Pharmacy from April 2023 to August 2023.*

Results: *Both RPR and HPR indices in the disease group were statistically significant lower than the control group ($p < 0.001$). The predictive value of rheumatoid arthritis of RPR and HPR with cutoff points of 0.016 and 0.455 respectively ($p < 0.05$). The RPR index was strongly positively correlated with HPR ($p < 0.001$). PLT was strongly negatively correlated with RPR ($p < 0.001$) and HPR ($p < 0.001$).*

Conclusion: *The RPR and HPR indices in RA patients were lower than those in controls, and could be one of the indicators to help assess inflammation in patients.*

Key words: *Red blood cell - platelet ratio (RPR), hemoglobion - platelet ratio (HPR), rheumatoid arthritis.*

I. INTRODUCTION

Rheumatoid arthritis is a chronic disease with a wide variety of systemic manifestations including persistent inflammatory synovitis, usually involving peripheral joints in a symmetric manner. Synovitis leads to cartilage damage and bone erosions and subsequently leads to changes in joint integrity. Clinical presentation varies from mild oligoarticular illness to relentless progressive polyarthritis with significant functional impairment [1]. RA affects 0.5-1% of adult population, this disease affects women three times more than men [2]. The inflammatory process affects the differentiation and development of erythroid precursors in the bone marrow, and the cytokines produced during this process stimulate the bone marrow to increase platelet production. There are few studies that have systematically assessed the association of PLT, RBC, Hb, red blood cells-platelet ratio (RPR) and hemoglobin-platelet ratio (HPR) with the disease activity of RA patients. And little is known about the diagnostic value of the peripheral blood PLT and RBC related indices in distinguishing

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between active RA and inactive RA. Therefore, this study aimed to describe hematological characteristics and the relationship of RPR and HPR indices with inflammation in patients with RA.

II. MATERIALS AND METHODS

2.1. Subjects

Patients fulfilled the 2010 ACR/EULAR criteria for RA [3] and agreed to participate in the study at the Department of General Internal Medicine - Endocrinology - Musculoskeletal at hospital of Hue University of Medicine and Pharmacy from April 2023 to August 2023.

Exclusion criteria: Patients who had hematologic diseases, other autoimmune inflammatory diseases, infections, malignancies, or had any history of other chronic diseases such as diabetes mellitus, dyslipidemia, thyroid dysfunction, severe liver or kidney impairment, those receiving treatment with corticosteroids within the last 3 months as well as not agreeing to join in the study.

Healthy individuals were recruited from the health examination center of the same hospital, and matched with RA patients for age and gender. At the end of the study, we selected 30 per group to participate in the study.

2.2. Methods

We conducted a described, cross-sectional study with convenience sampling. After being selected into each group, the study subjects will have blood drawn for testing. Complete blood cell (CBC) was performed on a Sysmex XN550 machine at the Department of Hematology. The study variables included gender, age, red blood cell (RBC), hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), Mean corpuscular hemoglobin (MCH), Mean corpuscular hemoglobin concentration (MCHC), white blood cell (RBC), neutrophils (Neu), lymphocytes (Lym), platelets (PLT), RPR, HPR.

Processed by SPSS 26.0 software, calculate mean, percentage and compare between groups with statistical significance when $p < 0.05$, predictive value of a variable is evaluated based on analysis Receiver Operating Characteristic (ROC) curve.

III. RESULTS

3.1. General characteristics of subjects

Table 1: Distribution by sex of study subjects

Group / Gender	Disease group	Control group
Male	6 (20.0%)	14 (46.7%)
Female	24 (80.0%)	16 (53.3%)
Sum	30 (100.0%)	30 (100.0%)

The female/male ratio in the case group was 4/1 while that in the control group was about 1/1.

Table 2: Age characteristics of research subjects

	Disease group	Control group
Age, mean ± SD	59.8 ± 10.8	37.7 ± 9.6
p	< 0.001	

There was a statistically significant difference in gender between the two study groups ($p < 0.001$).

3.2. Biological characteristics of the study group

Table 3: Number of peripheral blood cell lines of the study sample

	Disease group (n = 30)	Control group (n = 30)	p
RBC (1012/L)	4.0 ± 0.5	5.0 ± 0.7	< 0.001
Hb (g/L)	117.4 ± 11.3	139.7 ± 16.0	< 0.001
Hct (%)	36.4 ± 3.4	42.2 ± 4.3	< 0.001

	Disease group (n = 30)	Control group (n = 30)	p
MCV (fL)	91.0 ± 6.7	85.2 ± 8.7	0.006
MCH (pg)	29.4 ± 2.2	28.3 ± 3.4	0.151
MCHC (g/L)	332.5 ± 7.5	330.8 ± 10.7	0.001
WBC (10^9/L)	8.7 ± 2.4	7.1 ± 1.8	0.005
Neu (10^9/L)	6.0 ± 2.3	3.9 ± 1.3	< 0.001
Lym (10^9/L)	2.2 ± 0.7	2.6 ± 0.6	0.022
PLT (10^9/L)	320.9 ± 90.5	273.3 ± 62.9	0.021

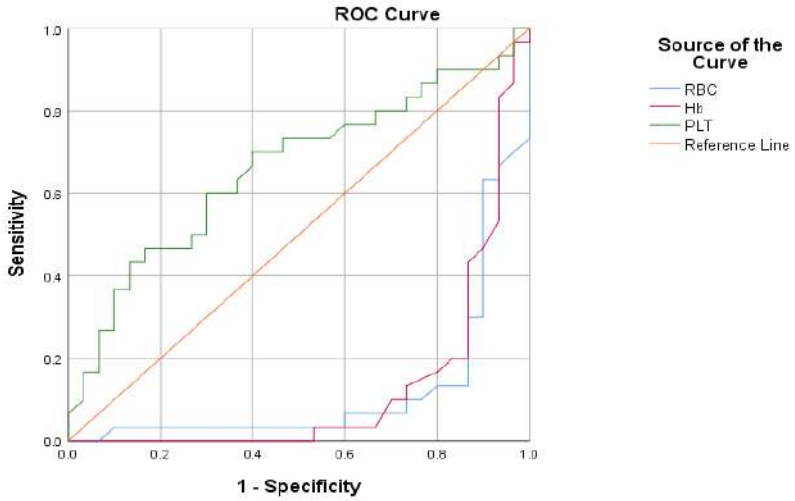
There was a statistically significant difference in the number of RBC, Hb, Hct, MCV, MCHC, WBC, Neu, Lym and PLT in the disease group and control group ($p < 0.05$). In contrast, MCH in the control group was not statistically different from the disease group ($p > 0.05$).

Table 4: RPR and HPR indices in the study group

	Disease group (n = 30)	Control group (n = 30)	p
RPR	0.014 ± 0.005	0.019 ± 0.006	< 0.001
HPR	0.400 ± 0.123	0.541 ± 0.147	< 0.001

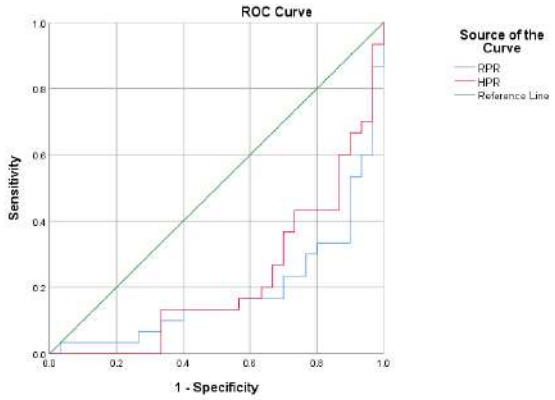
Both RPR and HPR indices in the disease group were statistically significant lower than the control group ($p < 0.001$).

3.3. Indices in predicting rheumatoid arthritis



	AUC*	Cut-off	Sensitivity (Se)	Specificity (Sp)	95% CI	p
RBC	0.120	4.39	0.133	0.133	0.026 - 0.214	< 0.001
Hb	0.125	129.5	0.133	0.267	0.030 - 0.220	< 0.001
PLT	0.659	292.5	0.600	0.633	0.519 - 0.799	0.034

Figure 1: ROC curves of RBC, Hb and PLT in predicting RA



	AUC	Cut-off	Sensitivity (Se)	Specificity (Sp)	95% CI	p
RPR	0.189	0.016	0.233	0.233	0.077 - 0.301	< 0.001
HPR	0.224	0.455	0.3	0.3	0.107 - 0.342	< 0.001

Figure 2: ROC curves of RPR and HPR in predicting RA

The predictive value of rheumatoid arthritis of RBC, Hb, PLT, RPR and HPR with cutoff points of 4.39, 129.5, 292.5, 0.016 and 0.455 respectively ($p < 0.05$).

3.4. Correlation between hematological indices in patients with RA

Table 5: Correlation between hematological indices in disease group

Hematological indices	RPR		HPR		PLT		WBC	
	r	p	r	p	r	p	r	p
RPR	-		0.930	< 0.001	-0.894	< 0.001	0.084	0.800
HPR	0.930	< 0.001	-		-0.930	< 0.001	0.064	0.735
PLT	-0.894	< 0.001	-0.930	< 0.001	-		0.001	0.998
WBC	0.084	0.800	0.064	0.735	0.001	0.998	-	

The RPR index was strongly positively correlated with HPR. PLT was strongly negatively correlated with RPR and HPR.

IV. DISCUSSION

4.1. General characteristics of subjects

In the results presented in table 1, our study has a female/male ratio of 4/1 while the control group was about 1/1. This result is epidemiologically consistent in that the disease affects women three times more than men [2]. Research of Essam T, et al. (2022) study on 60 RA patients showed that the female/male ratio was 6.5/1, quite similar to our study [4]. Uttam Biswas and colleagues (2020) showed that the female/male ratio was 4/1 when studying on 50 RA patients [5]. It can be explained by the fact that RA is an autoimmune disease, so it appears more in women than men.

The mean age of the patient group and the control group in our study was 59.8 ± 10.8 and 37.7 ± 9.6 years old, respectively, there was a difference in age between the control group and the patient group ($p < 0.05$) (table 2). The authors Essam T (2022), Li Xue (2022), Smyrnova Ganna (2014) also showed that the average age of the group of patients with RA was respectively 50.6 ± 8.8 [4], 57.11 ± 14.17 [6], 51.7 ± 10.3 [7], respectively.

4.2. Biological characteristics of the study group

In table 3, there was a statistically significant difference in the number of RBC, Hb, Hct, MCV, MCHC, WBC, Neu, Lym and PLT in the disease group and control group ($p < 0.05$). In contrast, MCH in the control group was not statistically different from the disease group ($p > 0.05$). The RBC, Hb, Hct and Lym indices in the disease group were lower than the control group, but the MCV, MCHC, WBC, Neu, PLT indices in the disease group were higher than the control group. In patients with RA, the chronic inflammatory process increases the production of inflammatory cytokines such as IL6, IL1β, IL-10, and IFNγ, which cause iron restriction, inflammation suppression of erythropoietic activity and decreased erythrocyte survival [8], finally causes anemia and reduces RBC, Hb and Hct. Chronic inflammation also stimulates the bone marrow to increase WBC, especially neutrophils (neu). At the same time, IL6 is a cytokine that stimulates the liver to increase thrombopoietin, thus increasing platelet production. Research by Li Xue et al (2022) on 178 RA patients including 88 inactive diseases (DAS 28 - CRP ≤ 2.7) and 90 active diseases (DAS 28 - CRP > 2.7); 164 patients as a control group showed that the group of RA patients had a higher PLT while the number of RBC, Hct and Hb were statistically significantly lower than the group control ($p < 0.001$). In addition, patients with active RA had higher PLT and lower RBC, Hct, and Hb with statistical significance compared to the group of patients with inactive RA ($p < 0.001$ or $p < 0.01$) [6]. A cross - sectional study by Manas Talukdar et al (2017) of 80 newly diagnosed RA patients presented significantly lower Hb and higher PLT, MPV in the highly active RA group compared to moderately active or inactive RA group ($p < 0.001$) [9]. A study by Aditi Patel et al (2022) on 20 newly diagnosed RA patients showed that 55% of chronic anemia, 27.5% iron - deficiency anemia; Patients with strong disease activity had lower Hb while PLT and MPV were statistically significantly higher than patients with moderate and low disease activity [10].

The results presented in table 4 showed that the RPR and HPR index in the disease group are 0.014 ± 0.005 and 0.400 ± 0.123, respectively, both statistically significantly lower than the control group (0.019 ± 0.006 and 0.541 ± 0.147) ($p < 0.001$). In the world, there are some studies that showed that the RPR and HPR in RA were lower than that of the control group, specifically, the author Li Xue's group reported the results of these two indices in the patient group as 0.019 ± 0.0065 and 0.55 ± 0.21, respectively, while the control group was 0.024 ± 0.0072 and 0.727 ± 0.23 ($p < 0.001$) [6]. As explained above, anemia and thrombocytosis are the result of chronic inflammation, so in patients with rheumatoid arthritis, the RPR and HPR values will be lower than normal.

4.3. RPR and HPR indices in predicting rheumatoid arthritis

In the research results, figure 1 and 2 both showed the predictive value of rheumatoid arthritis of RBC, Hb, PLT, RPR and HPR with cutoff points of 4.39, 129.5, 292.5, 0.016 and 0.455 respectively ($p < 0.05$). However, the AUC of the RBC, Hb, RPR and HPR indices is quite low so it is difficult to use to predict this disease. In contrast, the AUC of PLT has a higher value, so it will predict the disease better than the other indicators. It is possible that because of the small sample size of the study, the analysis has not yet covered the entire population. ROC curve analysis in the study by Li Xue and colleagues (2022) showed that PLT, RBC, Hb, RPR, HPR were able to predict severe disease activity with a cutoff point of 243 G/L (Se = 56.19%, Sp = 73.91%, AUC = 0.666, 95% CI = 0.591 – 0.736); 4.22 T/L (Se = 83.96%, Sp = 68.12%, AUC = 0.780, 95% CI = 0.711 – 0.839); 121 g/L (Se = 81.13%, Sp = 68.12%, AUC = 0.786, 95% CI = 0.717 – 0.844); 0.017 (Se = 74.29%, Sp = 68.12%, AUC = 0.744, 95% CI = 0.673 – 0.807); 0.48 (Se = 56.19%, Sp = 81.16%, AUC = 0.727, 95% CI = 0.654 – 0.791) [6].

4.4. Correlation between hematological indices in patients with RA

In our research, the RPR index was strongly positively correlated with HPR ($r = 0.930$, $p < 0.001$). PLT was strongly negatively correlated with RPR ($r = - 0.894$, $p < 0.001$) and HPR ($r = - 0.93$, $p < 0.001$) (table 5). Research by Li Xue (2022) also showed that PLT was positively correlated with DAS index 28 - CRP ($r = 0.327$, $p < 0.001$), CRP ($r = 0.284$, $p < 0.001$), ESR ($r = 0.331$, $p < 0.001$); RBC was negatively correlated with DAS 28 - CRP

index (r = - 0.428, p < 0.001), CRP (r = - 0.289, p < 0.001), ESR (r = - 0.481, p < 0.001); Hb was negatively correlated with DAS 28-CRP index (r = - 0.489, p < 0.001), CRP (r = - 0.341, p < 0.001), ESR (r = - 0.569, p < 0.001). RPR was negatively correlated with DAS 28-CRP index (r = - 0.31, p < 0.001), CRP (r = - 0.397, p < 0.001), ESR (r = - 0.329, p < 0.001). HPR was negatively correlated with DAS 28-CRP index (r = - 0.293, p < 0.001), CRP (r = - 0.402, p < 0.001), ESR (r = - 0.362, p < 0.001) [6].

V. CONCLUSION

Through research, we found that rheumatoid arthritis patients have lower RPR and HPR index than control group, the cutoff points of RPR and HPR index in predicting rheumatoid arthritis are 0.016 and 0.455, respectively. There is a strong positive correlation between these two indices and a negative correlation between platelets and RPR and HPR.

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Original research

THE KEYSTONE ISLAND PERFORATOR FLAPS: A NEW OPTION IN SOFT TISSUE MANAGEMENT OF PLASTIC SURGERY

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ABSTRACT

Background: *The keystone flap is an effective technique for reconstructive surgery that restores the natural contour of the affected area and provides superior aesthetic results. This technique involves taking healthy skin and subcutaneous tissue from a nearby area and transplanting it to the site of the defect, creating a new skin area that meets the patient's ideal outcome. We conducted a research project to objectively examine and evaluate the effectiveness and practicality of keystone flaps in clinical settings. Our two objectives were to analyze the characteristics of skin abnormalities on the body and to assess the surgical outcomes of using keystone flaps to repair defects.*

Methods: *40 patients with soft tissue defects throughout the body who underwent surgical treatment using keystone flap coverage at the Orthopedic and Plastic Surgery Center, Hue Central Hospital - Viet Nam.*

Results: *The most common causes of soft tissue defects are infectious necrosis (35.0%), chronic ulcerative lesions (32.5%), trauma (17.5%), scar excision (12.5%), and other factors (2.5%). Flaps are primarily designed in Type I and Type III fashion. Our follow-up evaluation of the flaps after 3 - 6 months showed that the majority of cases achieved good results, with 37 out of 40 cases (92.5%) and 3 out of 40 cases (7.5%) categorized as fair. No significant complications were reported.*

Conclusion: *The keystone island perforator flap is a modern method in plastic surgery that has proven to be a useful tool. The authors strongly recommend the use of the keystone technique as a safe, reliable, and feasible approach to covering soft tissue defects that vary in clinical characteristics.*

Keywords: *Keystone island perforator flaps, plasstic surgery, soft tissue defects.*

I. INTRODUCTION

According to Oswaldo et al [1], plastic surgeons have come a long way to find a reconstructive strategy that provides living tissue in order to restore both form and function following a wide range of congenital or acquired defects [2]; is versatile for any reconstructive requirement [3]; provokes minimal or no aesthetic or functional morbidity of donor areas [4]; entails short surgical times; and is replicable, with short learning curves and without large infrastructure requirements [5].

Closure of the skin defect following excision of skin cancers is ideally achieved by transposing local tissues of similar qualities. In this regard, flaps are generally preferable to skin grafts because they have better color and contour and are associated with the reduction of donor site morbidity. Whereas small defects have never been a problematic issue, larger ones often pose a unique challenge to reconstructive surgery, requiring knowledge, experience, and time. Searching for a better solution for bigger defects closure, more than 30 years of research and operative experience by its originator Felix C Behan, the concept of Keystone Design Perforator Island Flap was invented based on the most contemporary knowledge of the vascularization of the skin and soft tissue overlying bones [3, 6]. The keystone flap properly restores the contour of the

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defect and produces superior aesthetic outcomes through the use of nearby skin and soft tissue, giving patients who need reconstructive surgery the ideal outcome. The keystone perforator flap offers a single fasciocutaneous flap for use in nearly every region of the body to achieve rapid and reliable fasciocutaneous coverage with minimal morbidity to the patient, good cosmetic, and good quality of life. As such, it is well suited to meet the needs of reconstructive surgeons in the future and should appropriately limit the use of free flap reconstruction to defects unsuitable for loco-regional reconstruction and assist in the management of free flap morbidity by assisting donor site closure [7]. To the best of our knowledge, this paper is the first one focused on this flap and aims to evaluate the outcome of keystone flaps to cover the soft tissue defects with the various clinical traits of wounds.

II. PATIENTS AND METHODS

2.1. Patients

Between January 2021 and May 2023, a total of 40 patients (27 men and 13 women), with an average age of 56.1 ± 21.8 years (range: 12 - 95 years) underwent KDPIF reconstructions to cover defects at various locations on the body in the Plastic and Orthopedic Center, Hue Central Hospital.

We conducted a retrospective review of the assessment of various factors, including demographic data, pre-operative clinical examinations (such as causes, locations, and sizes), intra-operative conditions (including the state of the underlying soft tissue defect, the type of flap according to Behan's classification (figures 1, 2, 3, 4), and the flaps' survivals), hospitalization time, complications, post-operative outcomes, and follow-up examinations. This information was gathered over a period of 3 - 6 months and used to create a research questionnaire. No colostomy was done for all pressure ulcer patients; patients with acute local infections or who refused to participate in the study were excluded.

The types of keystone flaps used are based on Behan's classification [3]: Type I: Primary defect less than 2 cm width; Lateral deep fascia remains intact. Type IIa: Defects greater than 2 cm (< 2cm - ≤ 5cm) and Division of deep fascia required to facilitate tissue mobilization. Type IIb: Defects greater than 2 cm (< 2cm - ≤ 5cm) but concomitant use of split-skin graft, reduces tension on flap margin. Type III: Large primary defect (5 - 10 cm) and two keystone flaps on each border of the defect. Type IV: Rotational keystone flap, useful in joint contracture or open fractures, and Flap is raised with up to 50% sub-facial undermining.

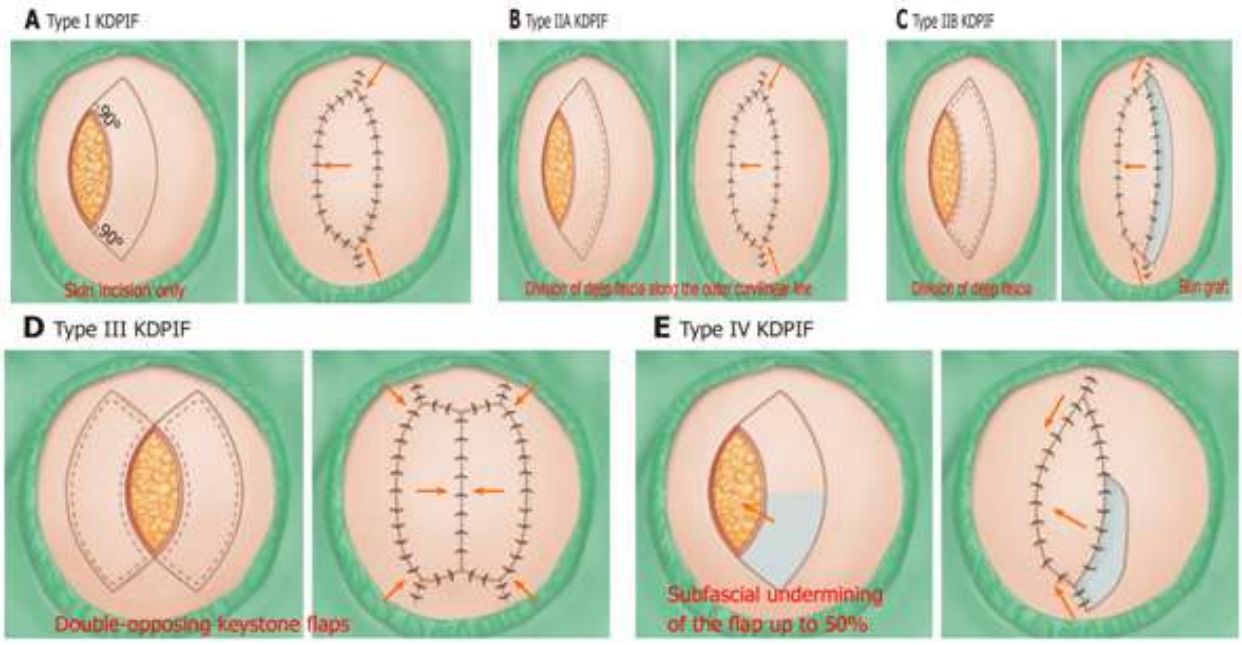

Figure 1: Keystone flaps according to Behan's classification

2.2. Surgical technique

- A handheld Doppler ultrasound machine, Model 811-B, with an 8.2 MHz probe, a measuring tape, and a marker pen to determine the course of adjacent perforator vessels and design the shape of the flap.

(A)

(B)

Figure 2: Identification of adjacent perforator vessels flap using a handheld Doppler ultrasound (A); measurement flap dimensions (B).

- Selecting the flap design based on the location, size, and characteristics of the defect, the following considerations can be made:

+ For small defects (width ranging from 2cm - ≤ 5cm), a simple keystone flap (Type I) is sufficient for coverage. Draw a line at a 90-degree angle at both ends of the defect and extend it in a manner that the length of the line is equal to the width of the defect in a 1:1 ratio. Connect the two endpoints with a curved line parallel to the edge of the defect. The width of the flap should be drawn in a 1:1 ratio to the width of the defect. The length of the flap is determined by the length of the elliptical-shaped cut.

Figure 3: Drawing a keystone flap design

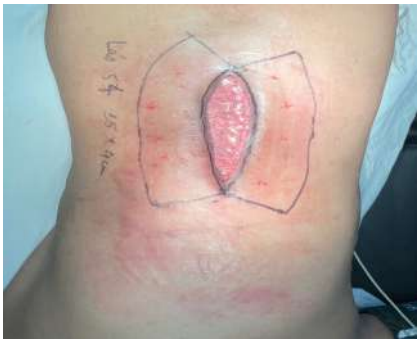

Figure 4: Drawing two keystone flap designs for back injury regions

+ For larger defects (width > 5cm), it may be necessary to design flaps using two keystone flaps (Type III and beyond) to achieve sufficient coverage. In this case, the second flap is designed symmetrically to the first flap, covering the remaining portion of the defect edge. The size of the second flap is designed similarly to the first flap.

- The operations were performed with the patients under general or local anesthesia.

- The surgical procedure consists of 4 steps:

Step 1: Preparation of the recipient site: Clear the inflamed, necrotic soft tissue and poorly perfused areas; Debride any inflamed or necrotic bone (if present); Measure the size of the defect and determine the desired reconstruction requirements.

Step 2: Harvesting the perforator flap: Skin incision according to the predetermined design; Deepen the incision by blunt dissection, protecting the perforator vessels and blood supply to the flap. In some cases, for small defects ranging from 2 - 5cm, it may not be necessary to dissect down to the subcutaneous layer.

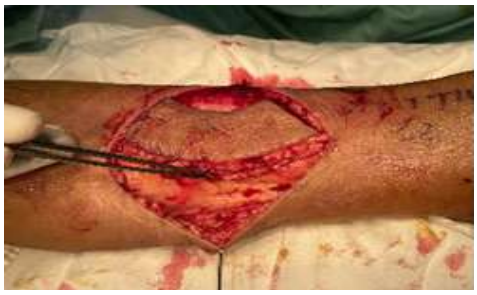

Figure 5: Elevation of the flap by following the marked keystone flap design

Step 3: Transferring and covering the defect with the flap: Depending on the initial design, whether it is a single flap or two keystone flaps, slide or advance the flap(s) to cover the recipient site; The first step is to suture the 'V' closure at the two distant corners (relative to the defect) of the keystone flap, transforming it into a 'Y' shape. This creates laxity of the tissue at the center of the flap, forming a right angle with the 'Y' shape and narrowing the secondary defect; Secure the flap using 3.0 or 4.0 nylon sutures with interrupted stitches. The distance between the stitches should be around 3 - 5 mm, avoiding overly thick sutures that may cause fluid or blood to pool under the flap; Place a drainage tube beneath the flap if necessary and maintain drainage for 48 to 72 hours (if applicable).

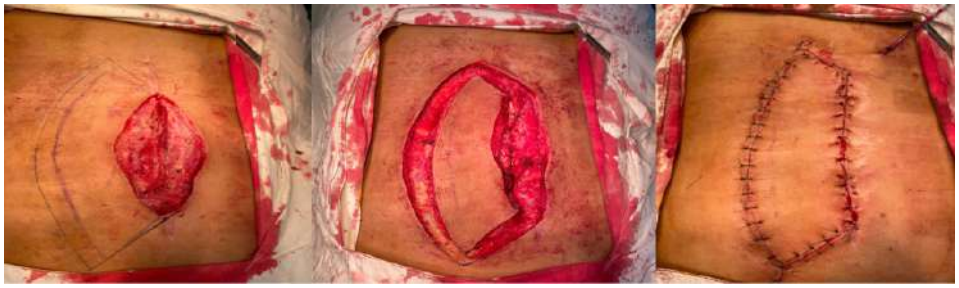

Figure 6: Flap sliding, V-Y closure, and closure of the flap.

Step 4: Assess coverage and perform skin grafting if needed: In cases where the flap cannot completely cover the defect, additional skin grafting may be performed using moist gauze dressings; In cases where the flap completely covers the defect, clean the surface of the flap and sutured incision, and then dress the surgical wound.

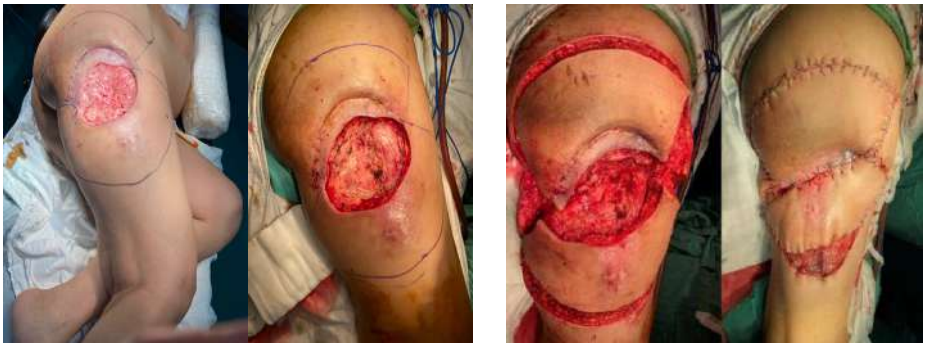

Figure 7: Additional skin grafting in Keystone flap type III

2.3. Statistical analysis

Data is recorded on a standardized research form and entered into Microsoft Excel 2016 software. Statistical analysis of the research data is performed using SPSS 20.0 software. Results are presented as means, percentages, and other relevant statistical parameters: percentage, mean, and variance calculations are used. Significance level: $p < 0.05$ with 95% confidence interval.

III. RESULTS

The results indicate infectious necrosis (35.0%), followed by chronic ulcerative lesions (32.5%), trauma (17.5%), scar excision (12.5%), and others (2.5%). Among the 40 cases, soft tissue defects vary in size depending on the extent of the injury. The smallest defect square measures 1.5 x 1.5 cm on the face, while the largest defect measures 18 x 10 cm in the buttock/pelvic region. The average area square is 59.5 cm^2.

The study sample recorded 3 cases (7.5%) with diabetes mellitus as a comorbidity. No cases of vascular diseases were reported, while the remaining cases either had unrelated comorbidities or had no associated diseases (92.5%).

There were 6 cases of large soft tissue defects located in the gluteal/pelvic and trunk regions, which required the use of 2 keystone flaps for coverage. The average flap area was 62.4 cm^2.

All the defects were reconstructed in a single-stage procedure by applying the keystone island perforator flap; the most frequently applied flap was the Type II A, B (n = 29), followed by Type III (n = 7), Type I (n = 3) and Type IV (n = 1) respectively.

The average hospital stay was 26.1 ± 14.4 days, with a minimum of 9 days and a maximum of 75 days.

All 40 patients had been followed up to evaluate the outcome over a three-month period after their discharge. The shortest follow-up time was three months, and the longest was 24 months. Out of the 40 cases, 37 (92.5%) showed stable healed scars and soft, pliable flaps, categorized as good results. There were 3 cases (7.5%) with fair results, including 3 cases with flap hypertrophy. Injuries in the head-face-neck region, lower extremities, and trunk achieved good results (100%). Injuries in the buttock/pelvic region showed good results (75.0%), fair results (25.0%), and no poor results.

IV. DISCUSSION

Evaluating the results of the keystone flap technique, based on clinical application in treating soft tissue defects, we have clinically identified several outstanding points of view:

The keystone flap has a high survival rate of 100%, providing favorable aesthetic outcomes, lower technical complexity, and reduced morbidity at the donor site. Based on the criteria of Oberlin C and Duparc J to evaluate the flap outcome, we obtained the following results: 38/40 (95.0%) flaps had good color and vitality; 2/40 (5.0%) flaps were hypotrophic, of which 1 case had water blister formation on the surface and required skin grafting, and 1 case had partial necrosis at the flap edge (< 1/3 of the flap area) without the need for second surgery; no complete flap necrosis observed.

The keystone flap method can be applied to large defects on the trunk and extremities without the need for complex surgical techniques or prolonged surgery while still achieving effective initial wound healing. It does not require sacrificing muscles or major blood vessels in the donor area, helping to preserve the integrity of muscles, blood vessels, and reduce the risk of complications. In this study, the defects varied in size, ranging from the smallest of 1.5 x 1.5 cm resulting from scar excision on the facial area, to the largest software defect of 18 x 10 cm caused by a chronic ulcer with tissue loss. The average surface area of the software defects was 59.1 ± 77.5 cm^2. Specifically, in our study, there were four large software defects in the amputation region and 2 in the trunk area with a size of 100 cm^2, resulting in an average defect area of 110 cm^2. Large and moderate software defects can be addressed by designing two keystone flaps on both sides of the defect, allowing for a sufficiently large skin flap to cover the wound and protect the underlying structures, including nerves, muscles, and penetrating vessels. This design has the advantage of completely closing the software defect without affecting the surrounding tissue, thereby enhancing aesthetics, reducing postoperative pain, and facilitating rapid patient recovery. Our study successfully covered six cases of large surface area defects using two keystone flaps.

In our study, the average hospital stay after surgery was 26.1 ± 14.4 days, with the shortest duration being nine days and the longest 75 days. Prolonged hospital stays were due to preoperative processes requiring infection control measures, such as VAC (Vacuum-Assisted Closure) therapy, to optimize the wound bed for flap surgery, or patients with underlying diabetes requiring intensified care, or patients with poor general condition and multiple comorbidities, necessitating a longer recovery time after surgery.

The evaluation of the flaps over three months with criteria such as vitality, mobility, softness, and the presence of complications like hypertrophic scars or recurrent inflammation showed that the majority of cases achieved good results, with 37 out of 40 cases (92.5%) categorized as Good, and 3 out of 40 cases (7.5%) categorized as Fair. There were no cases with Poor outcomes. Comparing our results to some findings by other authors worldwide: According to a retrospective evaluation conducted by Aravind L. Rao and Rakesh K. Janna, who studied 20 patients undergoing Keystone flap reconstruction for various defects from 2012 to 2014, the overall success rate of the flaps was 95% [8]. Another study by Joseph Khouri and colleagues assessed Keystone flaps for reconstruction of large trunks and upper limb defects in 28 patients, achieving a successful reconstruction rate of 97% [9]. The overall survival rate of the flaps was recorded as 100% in our experience.

V. CONCLUSION

In summary, the keystone surgical technique is a valuable tool for surgeons to create future aesthetic figures with various keystone variations. The authors encourage the use of the keystone method as a safe, reliable, and feasible approach in the treatment of soft tissue defects. However, the keystone flap also has some limitations: Performing keystone flap surgery requires a Doppler ultrasound device to determine the location of perforating vessels on the skin in the donor area. But, not all surgical facilities are equipped with this tool. Therefore, performing keystone flap surgery may encounter difficulties in accurately orienting the surgery. In addition, to the best of our knowledge, we take the liberty of making recommendations: this technique should be performed at specialized plastic surgery centers or large hospitals equipped with complete facilities and staffed by well-trained surgeons who have a high level of expertise and a thorough understanding of vascular and nerve anatomy, as well as soft tissue; Good coordination among the surgical team, anesthesiologists, surgical assistants, and physical therapy staff is necessary to enhance the quality and effectiveness of the surgery, minimize complications and adverse events, and ensure the safety and satisfaction of the patients.

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Original research

STUDY ON GAMMA GLUTAMYL TRANSFERASE CONCENTRATIONS IN PATIENTS WITH HEART FAILURE DUE TO ISCHEMIC HEART DISEASE

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ABSTRACT

Purposes: *Surveying serum Gamma Glutamyl Transferase levels followed by the grade of heart failure patients (according to the New York Heart Association - NYHA) due to ischemic heart disease and evaluating the relationship between serum Gamma Glutamyl Transferase levels with Heart failure staging and laboratory tests (NT-proBNP levels, (EF) ejection fraction) in heart failure patients due to ischemic heart disease.*

Method: *Study design: a cross - sectional descriptive study, including 140 patients were treated at the Department of Cardiology, Hue Central Hospital, from March 1st, 2021, to May 30th, 2022. They were divided into two groups: the group with heart failure (n = 70) and the control group without heart failure (n = 70).*

Result: *The serum Gamma Glutamyl Transferase concentration increased significantly in the group of patients with heart failure (56 U/l) compared with the control group (34 U/l) (p < 0.05). The median value of serum Gamma Glutamyl Transferase concentrations in heart failure stages II, III, and IV in the study according to NYHA classification was 53 U/l, 56 U/l and 286 U/l, respectively. Serum Gamma Glutamyl Transferase levels were positively correlated with the severity of heart failure according to the NYHA class, (r = 0.49; p < 0.001). GGT had good value in predicting the severity of heart failure (AUC = 0.869; 95% CI: 0.767 - 0.938), the best cutoff GGT ≥ 51 U/l with sensitivity: 81.25%, specificity: 77.27%; Gamma Glutamyl Transferase concentration had a moderate positive correlation with NT-proBNP concentration (r = 0.42; p = 0.0004) and had a negative correlation with left ventricular ejection fraction (LVEF), (r = -0.3; p = 0.013).*

Conclusion: *With a high diagnostic value, giving fast and accurate results of Gamma Glutamyl Transferase levels in various degrees of chronic heart failure, the Gamma Glutamyl Transferase test should be used as a good support test in the diagnosis and prognosis in patients with heart failure due to ischemic heart disease.*

Keywords: *Gamma Glutamyl Transferase, heart failure, ischemic heart disease.*

I. INTRODUCTION

Heart failure is the final consequence of cardiovascular diseases, which is currently a huge and urgent challenge for human health. So, it should be the concern and priority of many managers and scientists.

Worldwide, the rate of patients with heart failure is more and more increasing and the frequency of heart failure increases with age. In the United States, heart failure is the cause of hospitalization for more than one million patients each year and 50.000 patient deaths annually. Also in the United States, it is estimated that 4.9 million patients are treated for heart failure, 550.000 new heart failure patients annually. Heart failure is also a leading disease in the elderly. It is estimated that 6 to 10% of men or women over 65 have heart failure, and more than 80% of hospitalized heart failure patients are over 65 years old. Not only is it the most common disease, but it also occupies a leading position in the spending budget of the health sector [1].

Heart failure is not only the result of myocardial overload or damage but also the

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result of neurohumoral changes. In addition to classical morphological explorations in diagnosis, monitoring and prognosis, more recent interest has been focused on changes in serum concentrations of several biomarkers in patients with heart failure [2]. Today, assessing the degrees of heart failure and the effectiveness of treatment have been based on clinical signs and echocardiography. So, a more rapid and "non - invasive" method has been needed to diagnose and assess severity and prognosis in patients with heart failure.

Serum Gamma Glutamyl Transferase (GGT) is an analytical, inexpensive, easily performed and highly sensitive test that has traditionally been considered an indicator of hepatobiliary dysfunction and abuse of alcohol. Recent studies have shown its role in atherosclerosis and unstable plaque pathogenesis. Furthermore, epidemiological studies have identified a role for GGT in predicting the clinical progression of cardiovascular and cerebrovascular disease to life - threatening events such as myocardial infarction, stroke, and cardiovascular disease death, namely independent of the occurrence of liver disease, and alcohol consumption and as one of the risk factors. GGT is also correlated with cardiovascular risk factors, including diabetes, hypertension, dyslipidemia, and metabolic syndrome [3, 4]

In Vietnam, there had not been studies on GGT in cardiovascular disease and heart failure patients. Therefore, we conducted this study to investigate serum Gamma Glutamyl Transferase levels in patients with heart failure (according to the New York Heart Association - NYHA) due to ischemic heart disease and evaluated the correlation between serum Gamma Glutamyl Transferase levels with Heart failure stage and paraclinical symptoms (NT-proBNP levels, ejection fraction EF) in patients with heart failure due to ischemic heart disease.

II. MATERIALS AND METHODS

2.1. Research object

Study 140 patients was treated at the Department of Cardiology, Hue Central Hospital, from March 1st, 2021, to May 30th, 2022, and was divided into two groups:

- Diseased group: including about 70 patients with heart failure (diastolic and systolic heart failure) due to ischemic heart disease. Patients who are diagnosed with heart disease (hypertension, cardiomyopathy, valvular disease...), have clinical signs of heart failure (difficulty breathing, edema, hepatomegaly, distended neck veins...) are diagnosed as heart failure, and are graded according to NYHA criteria and the patient had coronary artery disease (Post sternal, transthoracic angina, pain radiating to shoulder, left arm, neck, and jaw accompanied by palpitations, anxiety, occurs with exertion, subsides with rest or nitrite, lasts several minutes and graded by the Canadian Heart Association (CCS))

- Control group: including about 70 patients without heart failure. Patients who come to the clinic or are hospitalized for other medical problems, have no clinical signs of heart failure, and the ejection fraction EF on echocardiography is within the normal range (EF $\geq$ 60%), with the same age as the patients in the group of diseases included in the control group of the study.

Exclusion criteria: patients with a history of chronic obstructive pulmonary disease (COPD) or patients with pneumonia, severe infection, diabetes, chronic renal failure requiring dialysis, acute myocardial infarction, acute heart heart failure.

2.2. Research methods

Cross - sectional descriptive research method. Convenient sample selection.

Research parameters: Hypertension was defined when the patient had a history of hypertension or systolic blood pressure $\geq$ 140 mmHg or diastolic blood pressure $\geq$ 90 mmHg. Diabetes: is defined when there is a history of diabetes or fasting blood glucose $\geq$ 7 mmol/l [5]. NYHA class of heart failure, grade IV was considered as severe heart failure. LVEF was classified in 3 groups: reduced EF (EF $\leq$ 40%), midly reduced EF (EF 41 - 49), preserved EF (EF $\geq$ 50%) [6].

Table 1: NYHA classification of heart failure [6]

Grade I	Does not restrict normal physical activity, does not cause fatigue, shortness of breath or palpitations
Grade II	Slight limitation of physical activity. The patient is well at rest. Ordinary physical activity leads to fatigue, palpitations, shortness of breath or chest pain

Grade III	Limit a lot of physical activity. Although the patient is well at rest, only mild exercise has symptoms
Grade IV	No physical activity without causing discomfort. Symptoms of heart failure occur immediately at rest. Just one physical exercise, the symptoms increase

III. RESULTS

There was no difference between the baseline risk factors between the diseased group and the control group, except that the frequency of diabetes patients in the diseased group (n = 22) was significantly higher than in the control group (n = 13), $p < 0.05$ (table 2). Regarding subclinical characteristics, proBNP and GGT concentrations were higher in the diseased group than in the control group, $p < 0.05$ (Table 3).

Table 2: General characteristics of the study sample

	Diseased group (n = 70)	**Control group (n = 70)**	**p**
Age (year)	72.33 ± 14.20	70.13 ± 10.07	> 0.05
Gender (male - n)	42	48	> 0.05
BMI (kg/m^2)	22.17 ± 3.67	22.36 ± 3.61	> 0.05
Hypertension (n)	56	58	> 0.05
Diabetes (n)	22	13	< 0.05
Coronary artery disease (n)	21	33	> 0.05
Smoking (n)	12	13	> 0.05

Table 3: Paraclinical characteristics of the study sample

	Diseased group (n = 70)	**Control group (n = 70)**	**p**
CT (mmol/L)	4.29 ± 1.58	4.24 ± 1.19	> 0.05
TG (mmol/L)	1.62 ± 1.09	1.93 ± 1.04	> 0.05
HDL (mmol/L)	0.97 ± 0.44	1.03 ± 0.35	> 0.05
LDL (mmol/L)	2.65 ± 1.29	2.36 ± 0.98	> 0.05
NT-proBNP(pg/mL) *	2262	144.6	< 0.05
GGT (U/l) *	56	34	< 0.05

*: non - normally distributed variable was presented as median

GGT concentration in NYHA class IV group was higher than other grades of heart failure ($p < 0.05$) (Figure 1). There was a moderate correlation between the degree of heart failure and the GGT concentration ($r = 0.49$, $p < 0.05$) (Figure 2). Analysis of the ROC curve to determine the best cutoff of GGT for severe heart failure, a GGT concentration greater than 51 U/l predicts severe heart failure with sensitivity: 81.25% and specificity: 77.27% (Figure 3).

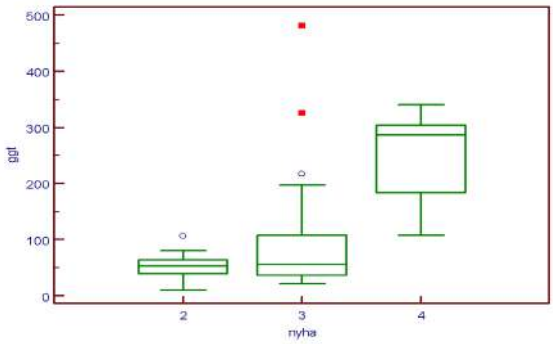

Figure 1: GGT levels according to the grade of heart failure NYHA

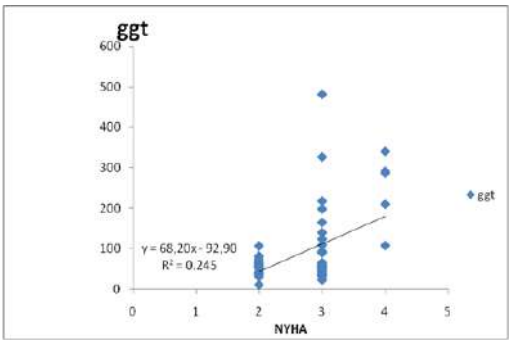

Figure 2: Correlation between the grade of heart failure and serum GGT

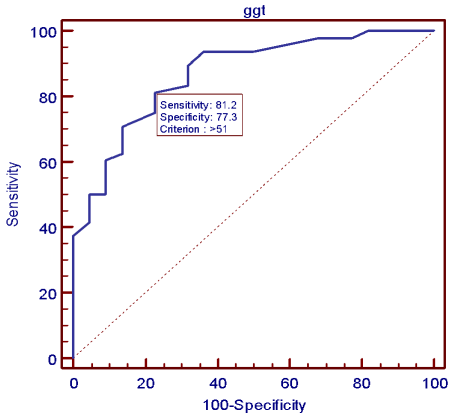

Figure 3: ROC curve of GGT in predicting severity of heart failure

AUC = 0.869 (95% CI: 0.767 - 0.938)

The concentration of Gamma Glutamyl Transferase has a moderate positive correlation with the concentration of NT-proBNP (r = 0.42; p = 0.0004) (Figure 4) and has a negative correlation with the ejection fraction index. LVEF (r = - 0.3; p = 0.013) (Figure 5).

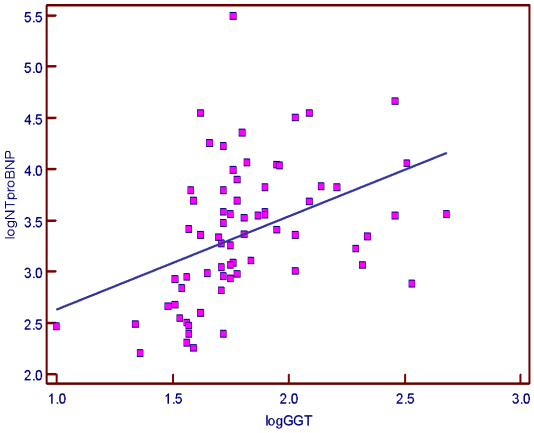

Figure 4: Correlation between NT-proBNP concentration and GGT concentration

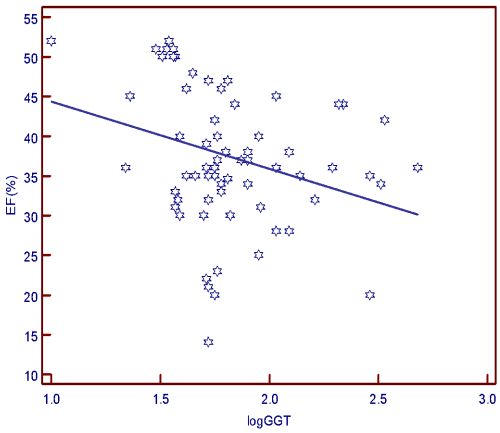

Figure 5: Correlation between LVEF and GGT concentration

IV. DISCUSSION

Chronic heart failure is a very common syndrome worldwide and is associated with significant morbidity and mortality. In addition to traditional risk factors, biomarkers of nervous system activity, inflammation, metabolism, and renal and hepatic dysfunction are associated with severity and disease progression.

Serum Gamma Glutamyl Transferase (GGT) analysis is a highly sensitive, inexpensive and easy test. This is considered an indicator of hepatobiliary dysfunction and alcoholism. Recent studies have also shown the role of GGT in the pathogenesis of atherosclerosis and atherosclerotic plaques [7]. Furthermore, epidemiological studies have demonstrated GGT in predicting cardiovascular and cerebrovascular disease risk factors, such as myocardial infarction, stroke, and cardiovascular mortality, independent of the occurrence of liver disease, and alcohol intake particularly. GGT also correlates with the most cardiovascular risk factors, including diabetes, hypertension, dyslipidemia, and metabolic syndrome.

In our study, the more severe the heart failure, the higher the GGT concentration. Several studies have consistently shown that serum GGT levels, mainly within the normal range, are most strongly associated with cardiovascular risk factors and predict the development of cardiovascular disease, hypertension, stroke, and type 2 diabetes. In patients with stable symptoms of heart failure, elevated serum GGT levels were significantly associated with the severity of heart failure [8,9]. Although the underlying mechanism for this association is unknown, several explanations for this phenomenon can be considered. Congestion in the liver is a clear mechanistic explanation for the increased levels of GGT in heart failure. Many studies have suggested that severe heart failure often leads to a congestive state of the liver, thereby causing liver enzyme stasis with high concentrations of GGT and bilirubin or local ischemia, and cytokine release may be involved in this process. However, there is still no convincing evidence for a definite or exclusive correlation between GGT, right atrium and pulmonary artery pressure, and severity of decreased cardiac output. Therefore, besides hepatic obstruction and/or ischemia, other factors that contribute to elevated GGT in heart failure must also be considered. Also, GGT is a marker of increased oxidase stress has been linked to the pathogenesis of coronary arterial disease by way of oxidant/antioxidant imbalance and inflammation [10].

According to our study, GGT concentration has a negative correlation with left ventricular ejection fraction index LVEF with a correlation coefficient of r = - 0.3. This further demonstrates that the more the heart function (specifically the left ventricle) declines, the more severe the heart failure is, leading to congestive liver conditions due to heart failure. It is a problem that has caused an increase in GGT. Our results are consistent with the results of foreign authors, especially the results of Gerhard Poelzl et al.: with the correlation coefficient between EF and GGT being r = -0.1 and $p < 0.05$ [7].

In our study, NT-proBNP and GGT concentration had a moderate positive correlation with a correlation coefficient of r = 0.42. NT-proBNP is a biomarker, and the mechanism of secretion of (NT-Pro) BNP is primarily from myocardial wall tension, increased ventricular filling pressure, and volume overload [11,12]. (NT-Pro) Plasma BNP is increased in patients with heart failure and is positively correlated with left ventricular filling pressure [13]. Therefore, for patients with severe heart failure corresponding to the higher NYHA class of heart failure, the greater the secretion of NT-ProBNP. Thus, along with the gradual increase of heart failure according to the NYHA class, NT-ProBNP also increased in a significant way. Therefore, NT-proBNP levels are correlated with GGT levels in patients with heart failure. This is especially meaningful in assessing the severity of heart failure based on NT-ProBNP and GGT, thereby having appropriate attitudes and indications for treatment as well as prognosis for patients.

V. CONCLUSION

With a high diagnostic value, giving fast and accurate results of Gamma Glutamyl Transferase levels in various degrees of chronic heart failure, the Gamma Glutamyl Transferase test should be used as a good support test in the diagnosis and prognosis in patients with heart failure due to ischemic heart disease.

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Case report

SEVERE CONGENITAL NEUTROPENIA CAUSED BY THE ELANE GENE MUTATION IN A 4-YEAR-OLD VIETNAMESE GIRL

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ABSTRACT

Severe congenital neutropenia (SCN) is an exceptionally rare genetic disorder associated with life-threatening bacterial infections. Among the several genetic variations related to SCN, heterozygous mutations in the ELANE gene encoding neutrophil elastase account for approximately 40 - 55% of the genetic causes. Herein, we present the first documented case of SCN in a Vietnamese girl from the Central region of Vietnam. The diagnosis was confirmed through genetic analysis of the ELANE gene, a known causative gene in SCN. The patient exhibited severe neutropenia and a history of recurrent infections that did not respond well to treatment. Treatment involved the administration of granulocyte-stimulating factor (G-CSF) and antibiotics, resulting in a successful increase in neutrophil counts. This report contributes to the understanding of SCN's clinical presentation, diagnosis, and management, particularly in regions with limited documented cases.

Keywords: *Neutropenia, severe congenital neutropenia, ELANE mutation.*

I. INTRODUCTION

Congenital neutropenia, a rare genetic disorder, can be categorized into two primary subtypes: Severe congenital neutropenia (SCN) and Cyclic neutropenia (CN) [1]. Typically, severe congenital neutropenia (SCN) is defined by extremely low absolute neutrophil count (ANC) (< 0.5 x 109/L for at least three months) and recurrent life-threatening bacterial infections [2]. The incidence of SCN is estimated to be 1 in 200,000 individuals [3].

Among several associated genetic mutations, heterogeneous mutations of the ELANE gene have been associated with both SCN and CN. ELANE mutations are known to correlate with more severe neutropenia and serious manifestations in SCN [4, 5]. In fact, ELANE mutations are the most recognized cause of congenital neutropenia and account for 40 - 55% of cases [1]. ELANE encodes a cytotoxic serine protease called neutrophil elastase, and over 200 ELANE mutations have been identified [3]. Most of the mutations (~80%) are missense mutations, although mutations that lead to splicing defects (~10%) and premature stop codons (~10%) also have been observed [6].

Reports of SCN originating from developing countries remain scarce, with few documented cases. The first reported case of SCN in Vietnam dates back to 2015 [7], followed by sporadic reports from various regions in the country. Additionally, clinical signs of this rare condition frequently overlap with those of other infectious diseases, leading to delayed or missed diagnoses. This report documents the first known case of SCN in a girl from Central Vietnam treated at Hue Central Hospital. The diagnosis was confirmed through mutation analysis of the ELANE gene, with the goal of improving SCN diagnosis and management through this report.

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II. CASE PRESENTATION

A 4-year-old girl was admitted to Hue Central Hospital because of a cough and high fever (39 - 40^0C). She had been treated at home with oral Cefuroxime (a 2nd Cephalosporin) for 4 days, but her symptoms did not improve. Upon clinical examination, she exhibited pale skin, rapid breathing, and moist crackles in both lungs. Her liver and spleen were not enlarged, but there was noticeable enlargement of neck lymph nodes.

Laboratory tests: Hemoglobin level of 9.5g/dL, white blood cell count of 5.3k/µL, neutrophil count of 0.0k/µL, lymphocyte count of 2.9k/µL, monocyte count of 2.2k/ µL, C-reactive protein (CRP) level of 83.1mg/L. The x-ray showed bilateral lung infection and moderate right pleural effusion (Figure 1). Because of the severe infection and neutropenia, the patient's medical history was collected and analyzed to evaluate. Her previous history of neutropenia or neutrophil count was unknown. However, she had experienced recurrent respiratory tract infections, otitis media, and gastrointestinal infections that did not respond well to anti-infection therapy. Specifically, she had otitis media at 9 months, followed by severe community-acquired pneumonia when she was 12 months old. Afterward, she experienced frequent episodes of respiratory infections and oral fungal infections, averaging around 7 to 8 episodes per year.

Two months prior to this admission, she had another episode of severe pneumonia with complications, including pleural effusion, and she received treatment for one month. Approximately one month before hospitalization, she had chickenpox and has since recovered. She had not been vaccinated against influenza and pneumococcal disease and was not taking any medications or toxins. Her family had no recorded history of allergies, asthma, blood diseases, or recurrent infection conditions.

Numerous tests were performed to determine whether her neutropenia was congenital or acquired. Tests for infection-related neutropenia were mostly negative. Viral serologies for CMV, HSV, EBV, and HIV were negative. Both blood culture and fungal culture also yielded negative results.

The hemogram results indicated several noteworthy findings: hypochromic anemia, a decreased white blood cell count, and an increase in two peripheral blood cell lines - platelets and monocytes. Bone marrow aspiration yielded no evidence of malignant cells and revealed reduced granulocyte proliferation. Further examinations, including tests for tuberculosis, hemophagocytosis, autoimmune diseases, and cancer, all returned normal results. Consequently, the possibility of acquired neutropenia was ruled out, leading us to focus on hereditary causes.

Given that certain primary immunodeficiencies can manifest as neutropenia, such as hyper IgM syndrome or Wiskott Aldrich syndrome, we conducted additional tests to exclude these disorders. Subsequent results indicated an elevated IgG level, specifically by 25.6 g/L. Serum titers of IgA and IgM, as well as the percentage of CD+ cells in flow cytometry, remained within normal ranges. Therefore, other immunological causes were entirely ruled out.

She received a regimen of broad-spectrum antibiotics, combining a 3rd cephalosporin with aminoglycoside, alongside antifungal prophylaxis. Additionally, subcutaneous injections of granulocyte-stimulating factor (G-CSF) were administered. Given the patient's medical history, it was deemed reasonable to initiate G-CSF treatment while awaiting genetic testing.

The initial G-CSF dosage was 5µg/kg/day for three days, followed by an increase to 6µg/kg/day for the subsequent five days. Unfortunately, there was minimal improvement in neutrophil levels compared to the first days of her admission, as depicted in Table 1, which illustrated the pre-and post-treatment changes in complete blood count.

The G-CSF dosage was incrementally raised every three days. Eventually, her neutrophil levels reached 3.47k/µL on the third day with around 8µg/kg/day of G-CSF. After a month of intensive treatment for severe neutropenia, during which she continued to receive G-CSF at a dose of 8µg/kg/day, the patient was discharged from the hospital in a healthy condition.

Table 1: Changes in the patient's complete blood count over the course of treatment.
[a] Before taking G-CSF. [b] After taking G-CSF.

Date	WBC (k/µL)	NEU (k/µL)	Hb (g/dL)	PLT (k/µL)
12/06/2023 [a]	5.3	0.0	9.5	280
13/06/2023 [a]	4.5	0.0	10.0	280
20/06/2023 [a]	6.2	0.1	10.1	572
26/06/2023 [a]	7.7	0.1	11.2	435
29/06/2023 [b]	4.9	0.0	11.9	289
30/06/2023 [b]	7.2	0.0	11.3	237
03/07/2023 [b]	7.4	0.2	10.5	178
06/07/2023 [b]	5.6	0.8	10.8	213
10/07/2023 [b]	9.45	3.47	10.8	319
27/07/2023 [b]	8.78	1.18	11.4	268

Genetic mutation testing results revealed that the patient's severe neutropenia resulted from a heterozygous mutation in the neutrophil elastase ELANE gene located on chromosome 19: c.242G > C (p.Arg81Pro). This mutation involved a change from G to C in the 242nd base, resulting in a codon alteration from Arginine to Proline. Consequently, the patient was diagnosed with severe congenital neutropenia (SCN).

Since her discharge, the patient has remained free of fever or signs of infection. G-CSF treatment continues, and she undergoes regular follow-up appointments to adjust the G-CSF dosage with the goal of maintaining an ANC within the range of 1.0 to 1.5x109/L.

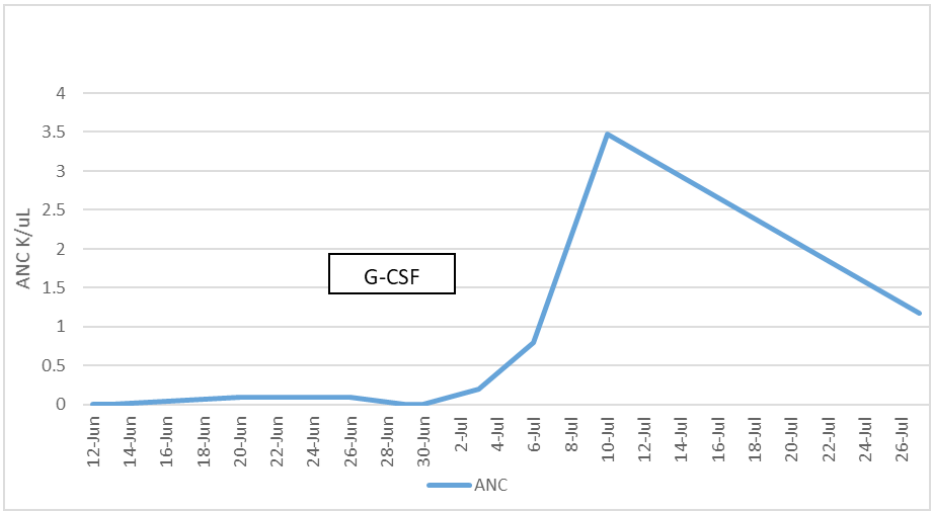

Figure 1: Absolute neutrophil count (ANC) during the first 2 months following the diagnosis of SCN, as influenced by G-CSF administration.

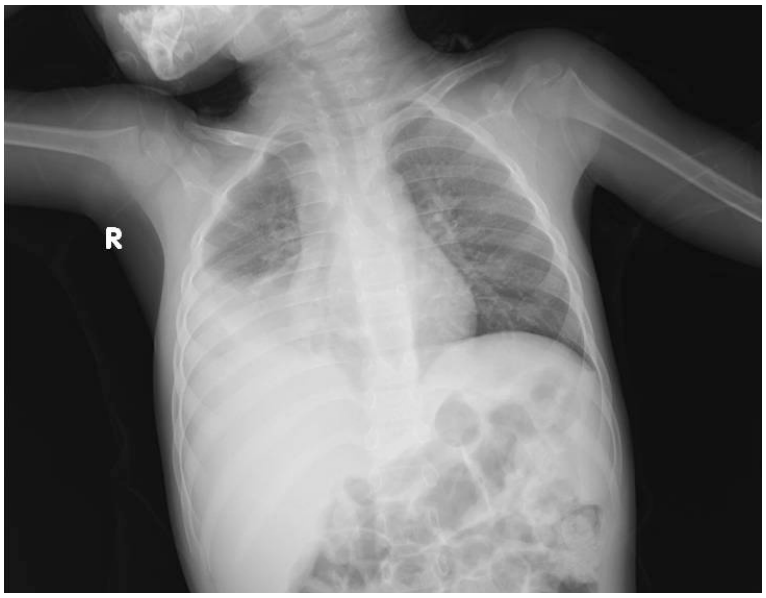

Figure 2: Chest X-ray at the time of admission

III. DISCUSSION

Severe congenital neutropenia (SCN), initially described in 1956, is a rare heterogeneous disorder characterized by an exceptionally low ANC (< 0.5x109/L for at least three months) associated with recurrent, life-threatening bacterial infections [2]. SCN encompasses a group of rare diseases that result from diverse defects in myeloid cell proliferation and maturation [4]. Cyclic neutropenia (CN) is another subtype of congenital neutropenia, characterized by neutropenia that typically recurs in a 21-day periodicity. Compared to CN, SCN is associated with more severe neutropenia and more serious clinical manifestations, and it confers an additional risk of developing acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS) [1, 3].

While the classical form of both disorders may be easily identifiable, a continuum of phenotypes occurs (i.e. variable length of neutropenia in CN or oscillating neutropenia in SCN), because the pathological mechanisms which result in the neutropenia affect both the degree of the nadir and the interval of fluctuations [4, 8]. If an ELANE gene mutation is present, the designation ELANE-related neutropenia or ELANE-associated neutropenia has been used, regardless of the pattern of variation in neutrophils [8]. It is unclear which factors determine whether a patient with an ELANE mutation will develop an SCN or CN phenotype, however, host factors and modifying genes have been proposed to play a role [4, 9].

Neutrophil elastase (NE) is a serine protease stored in the azurophilic granules of neutrophils along with other bactericidal proteins, and it plays a key role in host defense against bacteria [10]. NE is encoded by the ELANE gene on chromosome 19 and mutations in this gene have been implicated in both CN and SCN, with ELANE mutations seen in a majority of SCN and almost all CN cases [11]. Nowadays, more than 200 ELANE mutations have been identified [3].

Several hypotheses have been proposed to explain the pathogenic effects of NE mutations, one of which posits that the neutropenia is attributed to the accelerated apoptosis of neutrophil precursors secondary to mutant neutrophil elastase not being processed and packaged normally in the cell primary granules. The mutant enzyme impairs the survival of myeloid precursors through the initiation of the unfolded protein response, leading to programmed cell death and early-stage maturation arrest of myelopoiesis [9]

Horwitz et al. also proposes the mislocalisation hypothesis after demonstrating that mutant NE in neutrophils from patients with ELANE mutations

was mislocalised within the cell. They postulate this mislocation results in neutropenia as a result of induced endoplasmic reticulum stress which activates the unfolded protein syndrome with resultant apoptosis [11].

Diagnosis of ELANE-related neutropenia relies on the clinical presentation and companying history, serial measurements of ANC over a period of weeks, and demonstration of an ELANE gene mutation by molecular testing. A bone marrow biopsy is useful in assessing abnormalities in myelopoiesis and may be helpful in the demonstration maturation arrest. Karyotyping using conventional cytogenetics will help in demonstration of any chromosomal lesions that may be associated with specific syndromes if present. Additionally, it is crucial to rule out congenital malformations and investigate for extra haematopoietic system involvement to exclude other syndromes that are associated with neutropenia [8].

Management is multi-dimensional and includes treatment of manifestations of neutropenia (e.g. infections, fever, etc.), prevention of primary manifestations and secondary complications, as well as surveillance for malignant transformation. The introduction of G-CSF was a breakthrough in the treatment of congenital neutropenias and before its widespread use, patients regularly succumbed to life-threatening bacterial infections. The mainstay of therapy is daily subcutaneous G-CSF and vigorous treatment of infections. The goal is to maintain ANC > 1x109/L. It is recommended to start with a low dose of G-CSF (1-3 micrograms/kg/day). If the patient is not responding the dose can be increased. The majority respond well to G-CSF. Overall survival of individuals with SCN is estimated to exceed 80% [3]. However, since its introduction in 1998, G-CSF has attracted considerable attention owing to its potential risk of malignancy [12]. Recently, a strong relationship between G-CSF treatment and malignant transformation in SCN has also been reported [13]. Therefore, the dose, timing, and duration of G-CSF therapy should be very carefully determined in patients with congenital neutropenia, such as SCN and CN [3, 13]. Approximately five percent of patients do not respond even to higher doses of G-CSF. Haemopoietic stem cell transplantation should be considered in patients with refractory disease.

The girl we herein report showed typical manifestations of SCN including severe neutropenia and serious infection. ANCs have ranged from 0 to 3.47 k/µL due to the response of G-CSF. After excluding other secondary and primary causes of neutropenia, we thought much of this patient's severe neutropenia was due to genetic abnormalities. After the G-CSF (with the dose of G-CSF gradually increasing to 8 µg/kg/day) treatment, her neutrophil counts grew up, making mutations of the patient's G-CSF receptor gene less likely. To confirm the diagnosis of SCN, we sent out blood specimen to Gene laboratory for the Congenital Neutropenia Panel. The genes tested in the panel include ACTB, CSF2RA, CSF3R, CTSC, ELANE, G6PC3, GATA2, GFI1, HAX1, IFNGR2, LAMTOR2, LYST, RAC2, SLC37A4, SRP72, VPS13B, WAS. The ELANE gene is the most common gene alteration in SCN [4, 8, 14]. Finally, the gene result showed that in chromosome 19, there was a heterozygous mutation in the ELANE gene: c.242G > C 9p.Arg81Pro), with the change of G to C in the 242nd base, resulting in a change of the 81st codon (Arginine to Proline). This mutation has been reported to cause severe congenital neutropenia and cyclic neutropenia. So, this gene result is suitable for clinical manifestations.

IV. CONCLUSION

In summary, we report a child genetically diagnosed with Severe congenital neutropenia (SCN) due to ELANE mutation. This is the first case diagnosed in Hue Central Hospital and Central region of Vietnam. The case report may contribute to accumulating the number of SCN cases, which will help to expand the knowledge on clinical presentation, diagnosis, and management on this rare disease.

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Original research

EVALUATION OF THE ACCURACY OF IMPLANTS USING 3D PRINTED SURGICAL GUIDES IN IMPLANT PLACEMENT

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ABSTRACT

Background: *The optimal position of the implant in 3 dimensions in space is the most important factor to ensure the long - term success of dental implants. Today, advanced technology can simulate the virtual implant position before surgery. Through 3D printing technology, it is possible to transfer the virtual implant position to the surgical field using a static surgical guide. This study aims to evaluate the accuracy of 3D printed surgical guides when performing implant when performed using 3D printed surgical guides.*

Methods: *The study reports a series of clinical cases with 32 implants placed in the maxilla and mandible. The surgical guide is designed using Blue Sky Implant software. Postoperative CBCT data is combined with preoperative treatment plan data to evaluate deviations in implant position, angle between two implants, and vertical deviation.*

Results: *The study showed implant misalignment when using 3D printed surgical guides: misalignment at the implant neck was 1.11 ± 0.67 mm; at the tip is 1.43 ± 1.053 mm; The angle is 3.01 ± 2.53^o and the vertical is 0.71 ± 0.57 mm. The study noted that angular deviations, cervical, apical and vertical deviations were not statistically significant according to gender, parts of dental archs and implant position.*

Conclusion: *Using a surgical guide can help the implant to be placed more accurately in all 3 dimensions in the maxilla/ mandible. The 3D printed surgical guide has high precision and can be used to support implant surgery.*

Keywords: *Surgical guide, 3D, dental implants.*

I. INTRODUCTION

Dental implants are one of the increasingly popular tooth loss restoration methods due to their superior features compared to traditional tooth restoration ones. The important goal for successful implant placement is the ideal implant position in three dimensions in the maxilla/ mandible, long - term survival, and ensuring function and aesthetics. With the advent of cone beam computed tomography (CBCT) with its increasing availability, low radiation, low cost, preoperative three - dimensional implant planning is becoming more popular. The software enables virtual implant placement using digital data obtained from CBCT scans and intra - oral images of the patient, transferring pre - operatively planned implant positions into surgical guides (SG). 3D printing has improved implant treatment outcomes.

Many authors believe that using 3D printed SG in implant surgery brings many benefits, the implant is placed more accurately in all 3 dimensions in the bone, limiting the need for flap surgery or bone grafting, which leads to the fact that it helps to reduce costs, reduce trauma, and heal quickly [1]. Although implant placement techniques using SG are believed to be capable of achieving more precise and less invasive implant placement, this technique needs to be critically evaluated as it has been established in clinical practice, directly on the patient. Therefore, we conducted this study with the goal: Evaluate the accuracy of 3D printed surgical guides when performing dental implants.

II. PATIENTS AND METHODS

2.1. Patients

Including 10 patients treated with dental implants from February 2022 to August 2023 at

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the Department of High - Tech Dentistry - Odonto - Stomatology Center and Department of Cosmetic Dentistry, Cosmetic Center, Hue Central Hospital. The total number of research samples was 32 implant locations in the maxilla and mandible.

Patients who meet the following 3 criteria were included: (1) Patients aged 18 years and older. (2) The patient has lost teeth in the maxilla and mandible: Bone height ≥ 10 mm (mandible) ≥ 12 mm (maxilla) on CBCT film; Proximal and distal dimensions ≥ 6mm on CBCT film. (3) Patient agrees to participate in the study.

Exclusion criteria were: Having systemic diseases or local conditions that contraindicate dental implant surgery; Smoking > 10 cigarettes/day; The patient's mouth opening is limited to < 40 mm

2.2. Research method

We conducted a case series study on 10 patients with 32 implant positions

Research facilities: CBCT scanner, brand Willdem from Korea; The disk stores the patient's CBCT images as DICOM data (Digital imaging and communication standards in medicine); Trios 3 scanning system to convert function template data into digital data with STL data format (standard template library); Blue Sky Plan software is used to design dental implant surgery guides and evaluate postoperative deviations.

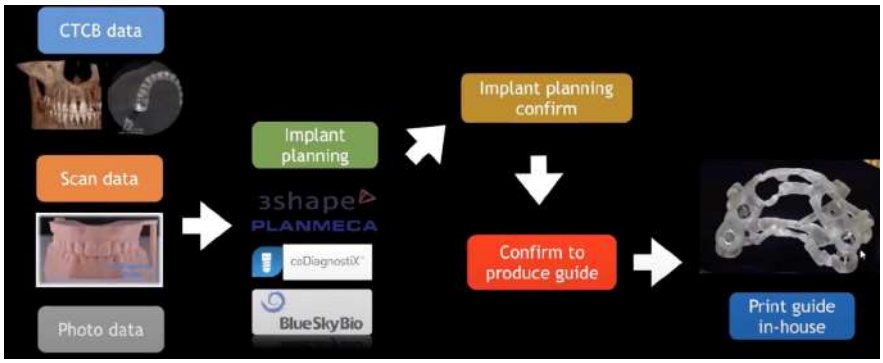

Figure 1: Clinic workflow [2]

Research content: The patient had an initial silicone impression taken before surgery. All plaster maxilla/ mandible samples were scanned using the Trios 3 scanning system to convert surface data of the samples into digital data in STL format (standard template library).

The patient had a CBCT scan before surgery, the data was saved in DICOM format and written to disk.

Using Blue Sky Plan software to combine 2 data including plaster samples and CBCT images of the patient. Then proceeding to plan treatment for the patients directly on this software. After designing a virtual tooth in the position where the implant needs to be placed to simulate the final restorations. Next, proceeding to place a virtual implant based on the final restorations above. From there, the appropriate position, size and direction of implant placement can be predicted. The implant surgery guide is designed based on the simulated implant position. After that, the surgical guides will be sculpted using a 3D printing system.

On the day of surgery, the surgical guide is tried on the patient, then the implant is placed based on the SG. The researcher is the person who directly place implants. All patients had CBCT scans performed after surgery and saved as DICOM data. Postoperative data is combined with simulated implant data when planning the SG design to evaluate accuracy.

2.3. Evaluation criteria

The accuracy of the surgical guide is evaluated by the deviation of the actual implant position after implantation compared to the virtual implant position when planning treatment (Figure 1) [3]. Implant deviations are evaluated including: deviations in the implant neck position (a), deviations in the implant tip position (b), vertical deviations (c) and angular deviations (α).

Determine the reliability and accuracy of the method.

To avoid measurement errors, all measurements were measured by the author under the training of a doctor specializing in reading and measuring CBCT images with many years of experience.

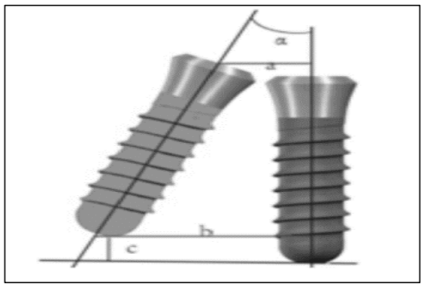

Figure 2: Figure depicting parameters for assessing implant misalignment [3]

Bone density: Misch CE, Kircos LT (1999) [4] classified the bone density into five groups based on number of Hounsfield units (HU). D1 corresponds to values greater than 1250 HU, D2 has 850 - 1250 HU, D3 refers to density within 350 - 850 HU, D4 has 150 - 350 HU and D5 less than 150 HU

Data processing: Data were recorded and analyzed using SPSS 26 software.

III. RESULTS

Table 1: Pattern of tooth loss and implant location

Pattern of tooth loss	Implant location	Ratio (%)	Patient	Ratio (%)
Complete maxilla + mandible	10	31,3	1	10
Complete maxilla	10	31,3	2	20
Complete mandible	4	3,1	1	10
Single tooth loss	8	34,3	6	60
Total	32	100	10	100

10 patients with 32 implant positions, including 01 patient with 10 implant positions in the entire maxilla and mandible, 01 patient with 06 implant positions in the entire maxilla, 01 patient with a full implant of the maxilla with 4 positions and 1 patient with 04 implant positions in the mandible, 01 patient with 2 dental positions R11, R21, 5 patients with 06 implant positions in the posterior mandible.

In the study sample, 15 (46.9%) implants were placed in female patients and 17 (53.1%) implants were placed in male patients.

The overall average age is 52.28 ± 8.95 years old, with no statistically significant difference between men and women

Bone D3 type accounted for the majority with 18 positions accounting for 56.3%; following by D2 type with 13 positions accounting for 40.6% and only 1 position with D4 bone density accounting for 3.1%. Most implant locations had bone widths ranging from 6 - 9mm, accounting for 81.3% with 26 implant locations, and there were 06 locations with bone widths > 9mm with 18.7%.

Table 2. Description of implant diameter and length

Description		Length			
		10	12	14	Total
Diameter	3,6	4 (12,5%)	1 (3,1%)	2 (6,3%)	7 (21,9%)
	4,2	4 (12,5%)	13 (40,6%)	3 (9,3%)	20 (62,4%)
	4,8	2 (6,3%)	2 (6,3%)	1 (3,1%)	5 (15,7%)
	Total	10 (31,3%)	16 (50%)	6 (18,7%)	32 (100,0%)

Based on the bone characteristics of the intended implant areas, all implants selected in this research sample have lengths of 10mm, 12mm, 14mm, of which 10 implant positions are 10mm long, accounting for 31.3 %, 16 locations used 12mm implants accounting for 50% and 6 locations used 14mm implants accounting for 18.7%. In terms of diameter, implants with a diameter of 4.2 mm

accounting for the majority with 20 (62.4%) positions, implants with a diameter of 3.6 mm and 4.8 mm have a proportion of 21.9% and 15.7% respectively. The force achieved when implanting the implant recorded the group of 30 - 35 N/cm accounting for the majority with 20 (62.5%) positions, followed by the group > 35 N/cm with 12 (37.5%) positions, there are no cases with force < 20 N/cm.

Table 3: Deviation of real implants with simulated implants when planning to make a surgical guide

Deviation	Average ± Standard deviation
Angular deviation	$3,01^{o} \pm 2,53^{o}$
Deviation in apical position 1	1,43 ± 1,05 mm
Deviation in neck position	1,11 ± 0,67 mm
Vertical deviation	0,71 ± 0,57 mm

The actual implant position deviation compared to the computer plan in this study was 3.01^{o} in angle, 1.43 mm in apical position, 1.11 mm in implant neck position and 0.71 mm to the implant position vertically.

IV. DISCUSSION

Our study sample was performed on 10 patients with an average age of 52.28 ± 8.95 years. It can be seen that this age group is in the 40 - 59 age group, which is the group with the highest implant rate among all age groups (accounting for 57%) compared to the 20 - 39 year old group (accounting for 29%) and the group over 60 years old (accounting for 14%). Compared to other studies by Dam Van Viet (2013) [5] (42.2 ± 14.8 years old), Souza (2022) [6] (58.9 ± 15.1 years old) reported group distribution elder age (all over 40 years old). In the research group, the majority were patients with entire jaw tooth loss, so the majority of patients were 40-59 years old and had entire jaw tooth loss due to periodontal disease. Regarding gender distribution in the study, women accounted for 53.1%, which is more than men, accounting for 46.9%. This result is quite similar to studies by authors Demirkol et al (2019) [7], Bui Viet Hung et al (2017) [8] all reported a higher proportion of women than men. This result can be explained by the fact that women care more about dental and aesthetic issues than men.

Regarding the causes of tooth loss that make patients coming for examination and choosing dental implants, our research shows that periodontal disease is the leading cause, accounting for 71.09%, followed by tooth decay and trauma, with the rates of 18.8% and 9.4% respectively. This result is similar to many previous domestic studies such as the research of Bui Viet Hung et al (2017) [8], Ta Dong Quan (2019) [2]. This is consistent with epidemiology in our country, the rate of periodontal disease in the population is still high and is the main cause of tooth loss in the community. Next, the rate of tooth loss due to tooth decay is higher than due to trauma, while research by Ta Dong Quan (2019) [2] showed that tooth loss due to trauma was up to 25% higher when surveyed in the anterior teeth region.

Bone density is one of the important factors that determine the success of implants and is closely related to the position on the maxilla/ mandible. According to Misch, the distribution of bone density in the upper posterior teeth area is D1: 3%, D2: 50%, D3: 46%, D4: 1%. Bone density affects the decision to choose drill size, as well as the timing of loading the restoration force on the implant. In our study, bone D3 type was common (43.5%). Common in middle - aged and teenage groups, this is consistent with the age group distribution in our study, mainly in the 19 - 39 year old group. Following is bone D2 type, which accounted for 40.6%. These results are similar to the research of Bui Viet Hung (2017) [8]. D2 type bone is the most suitable bone for implant placement. The contact interface between cortical bone and the implant surface helps the implant to have good initial stability. At the same time, the medullary bone has many blood vessels to help increase healing, reduce restoration waiting time. The study only had 1 case of D4 bone (3.1%). D4 bone is a porous bone that is difficult to achieve initial stability, and when drilling bone, special attention should be paid to because the drill is easily deflected.

The study showed that all implant placement areas had bone widths ranging from 6 - 9mm (81.3%), this result is similar to the study of Braut (2014) [1] which recorded average bone width. The average is 7,652 mm at the first molars position and 8,604mm at the second molars position and there are 05 positions with bone width > 9mm, so most of the implants selected in the sample are implants with average diameter.

The force achieved when placing implants was recorded in the 30 - 35 N/cm group accounting for the majority with 20 (62.5%) positions, followed by the > 35 N/cm group with 12 (37.5%) positions. This result is almost similar to the study of Gultekin (2016) [9] with an ISQ value of 70 and the results of Schnutenhaus (2020) [10] with an average value of 63. Because in our study, most of the bone density is D2 and D3, which is a favorable bone density for implants to achieve good initial stability.

When evaluating the accuracy of the implant surgery guide, our study recorded an average deviation of the implant neck compared to the simulated implant with an average value of 1.11 ± 0.67 mm. This result is almost similar to the study of Ta Dong Quan (2019) [2] when conducting research on the anterior teeth group with an average value of 1.06 ± 0.65 mm and the study of Smitkarn (2019) [11] when performing implants for single tooth loss cases (with an average value of 0.9 ± 0.8 mm). However, this value is higher than Kholy's (2019) [12] study on plaster models with the average value when performing trays on 3 teeth being 0.562 ± 0.086 mm. This difference is due to Kholy's (2019) [12] research being performed on a plaster models, so there is no interference with the lips, cheeks, mouth opening or abnormal movements of the patient.

When evaluating the deviation at the implant tip, our study recorded an average value of 1.43 ± 1.05mm; Similar to the research of Smitkarn (2019) [11] with 1.5 ± 0.7 mm and Ta Dong Quan (2019) [2] with 1.29 ± 0.84mm; Similar to the study by Kholy (2019) with an average value of 1.195 ± 0.397mm. Regarding the vertical dimension, the average deviation value in this study recorded was 0.71 ± 0.57mm; relatively higher than the study by Ta Dong Quan (2019) [2] conducted in the anterior teeth area. This is because when performing implants in the aesthetic tooth area, it is often easier to see the position of the implant than in the posterior tooth area, especially in the lower second molars.

For angle deviation in this study, we recorded an average value of $3.01^o \pm 2.53^o$, almost similar to the study of Ta Dong Quan (2019) [2] with an average of $3.04^o \pm 0.97^o$ and that of Smitkarn (2019) [11] with an average of $2.8^o \pm 2.6^o$. This shows that the surgical guide still has some deviation compared to the simulated implant and this deviation is not in any specific direction. The reason for this discrepancy is due to having to go through many stages from treatment planning to the surgical process and collecting post - operative data, including: taking initial impressions, scanning plaster samples, and taking X-rays. CBCT optics, SG printing, tightness of the guide tube, influence of clinical factors (blood, saliva, mouth opening, patient movement during surgery), surgeon experience, and bias of the assessment method [9]. However, 3D printed surgical guidance systems have been proven to help reduce trauma, reduce surgery time, reduce post - operative pain and swelling complications, and have higher accuracy than hand - crafted or implanted systems. Implant grafting does not use SG.

In addition, digital surgical methods can design and manufacture temporary restorations based on the position of the assumed implant when planning, helping clinicians to attach immediate restorations after surgery. This is very significant in preserving and guiding soft tissue, reducing patients' embarassment as well as shortening treatment time. Implant surgery and attaching temporary restorations before and immediately after surgery are also the trends of modern dental implants. Besides, 3D printed surgical guides also have some limitations such as additional costs and pre - operative time.

V. CONCLUSION

Using a surgical guide can help the implant to be placed more accurately in all 3 dimensions in the maxilla/ mandible. The 3D printed surgical guide has high precision and can be used to support implant surgery.

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Case series

PRELIMINARY EVALUATION OF COMPLEX DECONGESTIVE THERAPY IN THE TREATMENT OF UPPER LIMB LYMPHEDEMA AFTER BREAST CANCER

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ABSTRACT

Background: *Secondary upper limb lymphedema is a common complication after breast cancer treatment. Among the treatment methods, conservative treatment with complex decongestive therapy brings positive results to patients and it is non - invasive.*

Methods: *Cross - sectional description of 7 cases diagnosed with lymphedema after breast cancer and treated with complex decongestive therapy. Assessment was based on limb circumference with 4 different measuring positions and Quick - Disabilities of the Arm, Shoulder and Hand (Q-DASH).*

Results: *The mean age was 58.4 (42 - 73), there was 1 patient in stage I, 5 patients were in stage II and 1 patient was in stage III. After 1 month of treatment, all patient's hand circumferences were decreased, of which 1 patient was returned to normal hand circumference. All 7 patients were decreased Q-DASH scores.*

Conclusion: *This technique can be widely applied to other patients with upper limb lymphedema after breast cancer. This study needs to be performed with a larger sample size to confirm effectiveness.*

Keywords: *Lymphedema, breast cancer, complex decongestive therapy, limb circumference, Q-DASH.*

I. INTRODUCTION

Lymphedema is a chronic disease caused by dysfunction of the lymphatic system, resulting from the accumulation of interstitial fluid containing high molecular weight proteins. Lymphedema is mostly the result of other causes (after cancer surgery, radiation therapy, infection, filariasis, etc.), only 5% is congenital (primary lymphedema) [1, 2].

Secondary lymphedema of the upper limb is one of the common complications in breast cancer treatment with the rate of 16.6% [3]. The number of axillary lymph nodes that are dredged after surgery, chemotherapy, and radiation therapy are the main factors promoting the occurrence of lymphedema, and nearly 90% of lymphedema occurs in the first 2 years after radiation therapy [4].

In addition to hand edema, other symptoms that can be seen in patients with upper limb lymphedema which are limited movement, weak hand strength, hand pain, tingling sensation, and numbness. They lead to upper limb function impairment and reduce the patient's quality of life [3].

There are currently two methods of treating lymphedema: surgery and conservation. Among them, conservative treatment is recognized by the International Society of Lymphology (ISL) as an effective non - invasive technique for patients. Specifically, complex decongestive therapy (CDT) includes the following steps: manual lymphatic drainage, compression bandage, skin care, physical exercise and hand elevation [5].

Treatment of upper limb lymphedema with CDT is performed in many countries around the world, but in Vietnam it is still not popular and not performed accurately. Therefore, we conducted this study to evaluate the initial effectiveness of applying the CDT method at our hospital.

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II. PATIENTS AND METHODS

2.1. Research subjects

Sample selection criteria: Patients were diagnosed with lymphedema of the upper limb after breast cancer treatment and came to the Department of Rehabilitation - Hue Central Hospital from March 2023 to July 2023.

Exclusion criteria: (1) Patients in mild stage 0, I [1] who were instructed on how to self - manual lymphatic drainage on the arm edema with limb elevation. As a result, the hands were decreased edema and returned to normal, were not included in the study. (2) The patients had an acute infection, heart failure, arterial occlusive disease.

All 7 patients were included in the study.

2.2. Research methods

Treatment protocol: The patients were treated by CDT method. Full combination of the following methods:

1: Manual lymphatic drainage (MLD) [5, 6]

Includes the following main steps: Step 1: Abdominal breathing. Step 2: Stimulating lymph nodes in the neck, axilla, groin, abdomen. Step 3: Activating to open borders. Step 4: Draining the lymph in the right direction to where the lymph nodes is not affected.

2: Compression bandage [5]

Wrap edema hand with a multi - layer bandage, the pressure was higher at the periphery, gradually decreasing to the center of the body, use a short stretch bandage. Wear the compression bandage all day and night, even when exercising. Remove the bandage when bathing, skin care, and manual drainage.

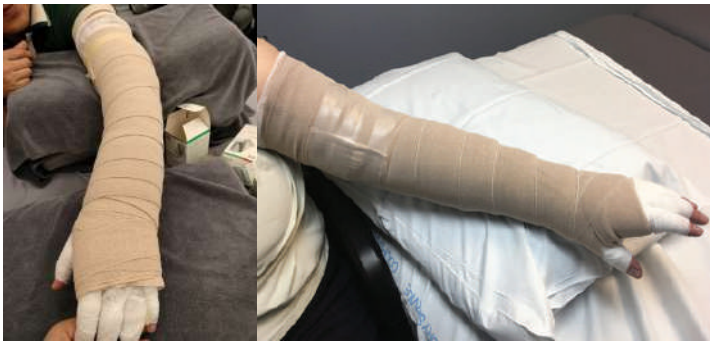

Figure 1: Compression bandage with short stretch bandage

3: Skin care

Always applied moisturizing lotion, moisturizing shower gel, and sunscreen when went out in the sun. In addition, you must also be careful in daily activities, avoided hurting your hands with edema.

4: Exercise and elevation your limbs

The patient was trained in mild to moderate intensity exercises. When practicing wore compression bandages or socks to increase efficiency. The patient was monitored and treated for 5 days at the hospital, then the patient and family members were instructed to continue performing the techniques at home. Re - examination after 1 month.

2.3. Evaluation criteria

Evaluation of the results was based on the change in arm circumference and the Q-DASH (Quick - Disabilities of the Arm, Shoulder and Hand) scale that assesses the function of the arm, shoulder and hand.

Measure the circumference with 4 landmarks.

- Arm: measure 10 cm up from the elbow crease, mark and measure the circumference through that point.
- Forearm: measure 10 cm down from the elbow crease
- Wrist: just below the processus styloideus ulnae.
- Hand: measure around 4 fingers (II, III, IV, V) from the base of the thumb

Limbs were measured at the time of examination and at re - examination after 1 month.

Measured in the morning, the patient is in a sitting position with his back straight and his hands placed on the examination table.

Q-DASH scale [7]

Is a self - assessment questionnaire consisting of 11 items, in which the answer options are presented in the form of a 5 - point Likert scale with

1 being "not difficult" and 5 being "impossible". Questions asked about difficulty in performing physical activities involving the upper limbs, pain, numbness, impact on social activities, work, and sleep. Total score ranges from 0 (no disability) to 100 (worst disability). The higher the score, the greater the likelihood of disability.

Rate this scale at the time of re-examination after 1 month.

III. RESULTS

During the period from March 2023 to July 2023, 7 patients with upper limb lymphedema after breast cancer were treated by CDT method. The median age was 58.4 (42 - 73), all females. The left/right breast cancer ratio was 6/1. There were 2 cases of breast cancer surgery combined with chemotherapy and 5 cases of breast cancer surgery combined with both radiotherapy and chemotherapy. Duration of breast cancer surgery: 1 patient under 1 year, 6 patients over 5 years. The time of upper limb lymphedema (up to the time of visit to the clinic) of all patients was less than 4 months, only 1 patient was 1.5 years. Stage of lymphedema: 1 stage I, 5 stage II and 1 stage III.

Triggering factors: 1 case of upper limb lymphedema after chemotherapy, 1 case after flying and vigorous upper limb massage, 1 case after heavy work, 4 cases of unknown triggering factors.

In addition to the symptoms of edema and thicker skin, 2 patients had upper limb edema pain, 1 patient had numbness, 2 patients had both upper limb lymphedema pain and numbness, no patient had signs of infection such as heat or red skin.

Table 1: Comparison of upper limb lymphedema circumference after treatment period

Numerical order	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Stage	**II**	**I**	**II**	**II**	**II**	**III**	**II**
ARM							
A	35	27	23	28	27.5	33.5	32
B1	41	28	34.5	31	30	39	34
B2	39	27	30	27.5	29	39	32
Decrease	2	1	4.5	3.5	1	0	2
FOREARM							
A	25	19.5	20	23	23.5	24.5	24
B1	35.5	21	27	25	26	35	29
B2	28	19.5	24	22.5	23.5	29	27
Decease	7.5	1.5	3	2.5	2.5	6	2
WIRST							
A	18	14.5	15.5	16.5	17	18.5	16
B1	23	18	19	18	18	23	20
B2	19	15	17	16.5	17	21	17
Decrease	4	3	2	1.5	1	2	3
HAND							
A	19.5	18	19	20	19.5	20.5	20
B1	21	22	20	22	21	22	24
B2	19.5	18	19	19.5	19.5	21	22
Decrease	1.5	4	1	2.5	1.5	1	2

A Measure the circumference of the non - edema limb at the time of examination (cm). B1 Measure the circumference of the upper limb lymphedema at the time of examination (cm). B2 Measure the circumference of the upper limb lymphedema at the re - examination after 1 month (cm).

At the time of examination, the upper limb lymphedema was larger in size than the corresponding healthy upper limb when measured in different positions. After 1 month of re - examination, upper limb edema circumference was decreased. The maximum reduction is 7.5 cm. There was 1 patient in stage I after 1 month of treatment, the upper limb edema circumference was returned to normal. In other patients in stages II - III, the upper limb edema circumference was decreased but was not returned to the normal level (except for 1 patient who lost weight, so the edema was decreased even more than the initial measurement of a normal upper limb).

Figure 2: A patient with stage II lymphedema after breast cancer at examination (A); After 1 month of re-examination (B).

Table 2: Comparison of Q-DASH score at the time of initial examination and the time of re - examination after 1 month.

Numerical order	1	2	3	4	5	6	7
Q-DASH initial examination	73	64	93	43	61	64	66
Q-DASH after 1 month re-examination	34	20	55	11	30	57	20

All 7 patients reduced their Q-DASH scores, 5 patients reduced their scores by more than 50%. All patients had improvements in upper limb function, reduced pain and numbness, improved sleep, work and activities daily.

IV. DISCUSSION

Breast cancer is one of the most common cancers in women. According to Globocan statistics in 2020, the global incidence of breast cancer in women was 24.5%, the highest among all types of cancer in women [8]. Methods to treat breast cancer can include mastectomy with axillary lymph node dissection, radiation therapy, chemotherapy, etc... which can all damage the lymph nodes and vessels, cause stagnation and fluid accumulation and lead to lymphedema in the upper limbs. Surgery or conservation are the two main methods of treating lymphedema. Surgical methods such as lymphatic-venous anastomosis [2], vascularized lymph node transplantation, liposuction [1] ... however, these are highly technical and difficult to perform, requiring

modern equipment. In contrast, conservative treatment with complex decongestive therapy is increasingly popular because it is noninvasive and easy to perform.

According to research by E. Michopoulos and colleagues, lymphedema time was one of the factors predicting the effectiveness of CDT treatment in patients with lymphedema [9]. 105 patients with lymphedema of an upper or lower limb were divided into 2 groups with edema for less than 1 year (A) and 1 group with edema for more than 1 year (B). Both groups received CDT intervention for 4 weeks. The effectiveness of CDT was determined by the percent reduction of excess volume (PREV) in the limb lymphedema compared to the healthy limb. Edema results decreased significantly in both groups but decreased more in group A ($p < 0.001$). Thus, duration of lymphedema was found to be a strong predictive factor that may significantly impact CDT efficacy. Therapeutic effects were increased in subjects who were detected and treated earlier for lymphedema. In our study, there was 1 patient in stage I who, after 1 month of re - examination, the circumference measurement returned to normal. The other patients in stages II and III had limb size measured after 1 month were decreased but has not returned to normal. One patient had lymphedema for 1.5 years and when she was re - examined, the arm circumference had not decreased, forearm and hand were decreased.

In the study by C.Basoglu et al., the purpose was comparing the effectiveness of CDT with Kinesiology taping (KT) on patients with upper limb lymphedema after breast cancer: a randomized controlled clinical trial [3]. Forty patients with stage 2 lymphedema after breast cancer were divided into 2 groups, 20 patients used CDT therapy, 20 patients used KT therapy. Re - evaluate after 1 month of treatment and 1 month of follow-up. Outcomes were based on limb circumference and volume, grip strength, upper limb function, and quality of life (with the Q-DASH and FACT-B Functional Assessment of Cancer Therapy-Breast). The study found that both KT and CDT significantly reduced edema limb circumference and volume, however KT was less effective than CDT in terms of reducing edema limb circumference, volume, grip strength, and quality of life. The results showed that KT with skin care and exercise was not a substitute for MDL and compression bandaging in the intensive phage of classic CDT.

The limitation of the study was the small number of samples. The patients in the study were treated and closely monitored for the first 5 days, then instructed to go home for treatment. However, when they came back home, the compression bandage and drainage may not be done correctly by the patient and their family.

V. CONCLUSION

Through 7 clinical cases, we found that complex decongestive therapy for the treatment of patients with upper limb lymphedema after breast cancer was a safe, non - invasive method that helped to reduce lymphedema of the arm circumference and improved function of upper limbs. This technique can be widely applied to other patients with upper limb lymphedema after breast cancer. This study needs to be performed with a larger sample size to confirm effectiveness.

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Case series

REVERSE HOMODIGITAL DORSORADIAL FLAP FOR THUMB SOFT TISSUE RECONSTRUCTION

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ABSTRACT

Primary and secondary reconstruction of the thumb is a common reconstructive challenge for the hand and plastic surgeons. Currently, The kite flap or the First dorsal metacarpal artery flap remains the regular choice and is believed to be the best for distal thumb defects, but it's the first time we have utilized a reverse homodigital dorsal radial flap for the thumb with an expected outcome. A 37 - year - old male patient suffered partially, obliquely, and radially necrotic thumb tip in the second week following conservation stitching of the wound due to a motorcycle accident. The necrotic tissues were desbrided and the residual defect was covered simultaneously by reverse homodigital dorsoradial flap. The Interphalange (IP) and Metacarpalphange (MCP) joints were flexible, and the active rang of motion (ROM) of the affected thumb was not limited at 3 months post - op. The reverse homodigital dorsoradial flap has become a useful and valuable material for thumb reconstruction. The flap provides acceptable aesthetic results with primary closure of the donor site and returns the essential functionality to the affected thumb.

Keywords: *Thumb, reverse homodigital dorsoradial flap, case report.*

I. INTRODUCTION

Hand function is very important in daily life, and work but it is also vulnerable to trauma, burn, or other injuries. The thumb plays the most important role in hand functionality. The pinch, grip, grasp, and precision handling are more easily accomplished with an opposable thumb. Soft tissue defects of the thumb, exposing tendons, nerves, arteries, or bone require a reliable vascularized flap reconstruction, preferably with a local or regional flap.

In the past, to resurface defects of the distal thumb, we have routinely selected the local vascularized flaps, of which the most popular has been the kite flap followed by the Brunelli flap. However, in this case, the palmar oblique defect radially to the distal thumb was well-suited to the utilization of a reverse homodigital dorsal radial flap, rather than a kite flap or a Brunelli flap.

The basic plastic surgery principle of altering "like with like" is still particularly true for thumb reconstruction. Soft tissue coverage of a thumb defect should be stable, pliable enough for easy movement, preserve length, and ideally protect at the minimum sensation [1].

Many reconstructive options for soft tissue coverage of a distal dorsal thumb defect include the following: skin graft (though grafting over exposed bone commonly results in an unstable closure prone to failure and breakdown secondary to pressure), reverse cross-finger flap, modified Moberg (palmar advancement) flap, first dorsal metacarpal artery flap (kite flap, Foucher flap), and Brunelli flap, reverse homodigital dorsoradial flap, or free flap.

The commonly employed kite flap has become the workhorse for sensory distal thumb reconstruction [2 - 4]. However, in a complex hand trauma at the place opposite to the index, and in which the donor site of the kite flap is no longer available, the reverse homodigital dorsoradial flap becomes the most suitable choice.

The reverse homodigital dorsoradial flap is nourished by a constant vascular axis raising from the radial artery (dorsoradial digital artery) and connecting with the arterial palmar circuit at the level of the middle third of the proximal phalanx [4] (Figure 1).

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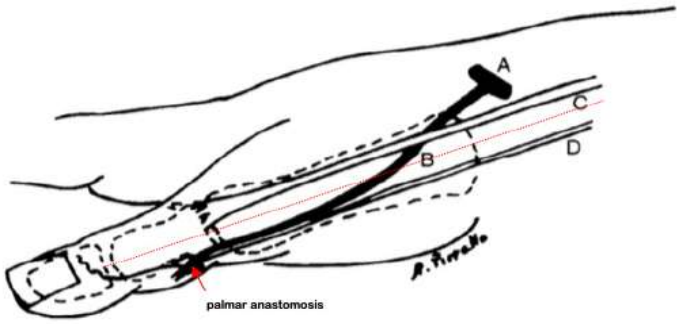

Figure 1: Anatomy of dosal radial collateral artery. A: radial artery; B: Dorsal radial branch; C: Extensor pollicis brevis tendon; D: sensory collateral branch of the radial nerve. The dorsal radial artery keeps an average distance from the median axis of the finger about 1 cm [5].

The digital dorsal radial artery divided by the radial artery at the grade of anatomical snuffbox ranging is measured from 0.6 mm to 0.8 mm in diameter and passes under the extensor pollicis brevis tendon. Then, it courses straight and regularly on a subcutaneous plane longitudinally on the radial side of the thumb toward the distal thumb and is far from the midline of the digit approximately 1 cm [5]. The artery constantly communicates with the palmar circuit at the level of the middle third of the proximal phalanx of the thumb. The pedicle involves the accompanying sensory branch of the superficial radial nerve running close to the artery, to provide a sensate flap. Care should be taken to a sufficiently wide dissection of subcutaneous tissue and to preserve visible larger veins to ensure adequate venous drainage of the flap, because no specific vein has been isolated or described as the main vessel for venous drainage, in the current literature [4, 6].

II. CASE PRESENTATION

2.1. Patient information

A 37 - year - old male patient was admitted to the hospital because of a wound to the left distal thumb a couple of hours after a motorcycle accident.

The patient had no history of smoking and no previous surgical intervention.

2.2. Clinical findings, diagnostic assessment

Recorded at clinical examination, the wound was in the crossed form on the pulp of the thumb, towards the radial side, contaminated by road dust, and poorly perfused at the peeled cutaneous island. The wound was shaped like a skin island. Flexor and extensor tendons were not damaged at the injured place. The x-ray images of the affected hand showed clearly that the bone was intact.

2.3. Interventions

In the first operation, he was made debridement to remove foreign bodies with intraoperative antibiotic therapy. We decided to stitch conservatively without revascularization after checking that the wound beds were still perfused and took him out of the hospital post - operation for 5 days. Unfortunately, he came back to us due to a partial necrosis of the remaining skin.

We planned to do a second debridement and reconstruct residual defects simultaneously. In the second operation, the necrotic tissues were excised and a defect was left on the radial side of the thumb exposing the bone of the distal phalanx (fig 2). Defect sizes were 3 cm and 2 cm in length and width, respectively. We decided to apply the reverse homodigital dorsoradial flap to resurface the defect.

Figure 2: The defect at the radial side of the distal thumb after the radical debridement

Figure 3: The designs of reverse dorsal radial artery flap (a red arrow) with its sizes were 5 cm and 3 cm in length and width, respectively.

Techniques of flap dissections: It can be useful to identify the course of the dorsal radial digital artery from the snuffbox to the middle point of the proximal phalanx by a hand - held Doppler. This point which will be the pivot point of the flap, is marked. The skin island was drawn on the dorsal radial side of the first metacarpal of the affected thumb. Its size is determined by the size of the defect, approximately 5x3 cm running parallel to the line from the snuffbox to the pivot point. (fig 3)

The surgical procedures were performed under brachial plexus anesthesia to avoid vascular injury nourishing the flap and the tourniquet was set up at the level of distal arm. An incised line was made from the proximal cutaneous island designed previously. The flap was raised from proximal to distal part by blunt dissection to avoid damaging the pedicle which consists of an artery and a sensory collateral nerve being very near the artery. The extensor pollicis brevis was determined and was gently spread apart (fig 4). The main artery and concomitant nerve were cut and coagulated, and then enclosed in the flap. The subcutaneous pedicle is taken and subdermal dissection is along the middle axis of the thumb toward the pivot point. It's not necessary to isolate the artery of the pedicle. We believe that the protection of adequate soft tissue around the pedicle allows a venous outflow though no real vein was identified. It is useful to include in the pedicle every venous skin branch seen near the pedicle to increase the venous flow. We didn't create a cutaneous tunnel to turn and transpose the flap to the receipt site to avoid the risk of venous congestion. A sufficiently wide strip of subcutaneous tissue has to be included to provide venous drainage and to avoid kinking of the pedicle. The proximal to distal dissection of the pedicle stopped at the midpoint of the proximal phalanx to protect the anastomosis with the palmar vascular network.

Figure 4: The dissection of the flap including a vascular and nervous pedicle, from proximal to distal, longitudinally the extensor pollicis brevis tendon (red arrow).

Figure 5: Image of flap at post - operative second week with a ruddy and elastic surface and tension - free edges.

After the flap is raised, the tourniquet is released to check adequate refills of the vascular pedicle and vascular flow to the flap and then rotated with an angle of 180 degrees and sutured with a few stitches. We cut the residual skin between the donor and the recipient site. Then the flap was stitched into the defect edges and the skin-skin closure between the cutaneous tail and the surrounding edges was performed, as well. The donor site then can be closed directly without a skin graft because of the small dimensions of the flap, and the skin elasticity.

2.4. Follow - up and outcomes

The thumb was immobilized with a short arm cast brace for 5 days. An IV cephalosporin 1st generation was prescribed 2 grams per day, every 6 hours. On the 10th day post - operation, the flap was still alive, ruddy, and had tension-free edges. After 2 weeks, the splint was removed and the patient was advised to move his thumb gently, and passively. Active exercises were allowed in the 4th week (fig 5). The patient had no numbness or paresthesia on the flap and could distinguish 2 points 5 mm apart. After two months, he could reach normal function of the thumb and come back his work after 3 months (fig 6).

He didn't complain about the scar created by the direct closures of the donor site.

III. DISCUSSIONS

Reconstruction of extensive defects of the thumb can be a difficult problem because immediate closure is of extreme importance for preserving function and avoiding complications. Many kinds of flaps have been described to recover these defects. The reverse homodigital dorsoradial flap is one such clever choice in this case with many dominant advantages. The flap transfer affects only one finger. The sensate recovery and the last scar are acceptable. In the dissection of the flap, the mobilization of its pedicle does not require the perishing of the most important artery. Moreover, reaching the dorsal or palmar distal thumb is the other favourableness of the flap with elastic, thin, and hairless texture on the surface. That good point creates a comfortable impression on the patient in the long term. Finally, postoperative care is simple and the mobilization of the unaffected fingers is intact. However, because venous drainage of the flap is not created by any specific vein, a congestive complication of the flap may occur. Therefore, a wide dissection of subcutaneous tissue and aponeurosis included into the island and a cutaneous tail added are the methods to improve adequate venous drainage.

The skin graft is not suitable for this kind of defect because it lacks the thick tissues required to cover the exposed bone and it's probable to secondary injury in the future. The cross - finger flap requires a staged approach on two fingers and a period of immobilization causing the risk of subsequent joint stiffness [6]. Moberg flap which was first described in 1964 and then modified by O'Brien in 1967 can reach up the pulp defects of the thumb measuring even 4 cm in length but it presents some limitations including the mobility of this flap is quite limited, the requirement of skin graft at proximal palmar thumb and first web space may cause a volar contracture [7]. Another option is heterodigital neurovascular island flaps based on palmar digital arteries and nerves but it requires extensive digital and palmar dissection for the mobilization [6]. A kite flap from the dorsal surface of the adjacent index finger that was first described by Foucher and Braun in 1979, may be chosen for the distal thumb defects. The disadvantages of this flap include a skin graft for the donor site and the involvement of two fingers. Furthermore, the relatively darker dorsal skin consisting of hair follicles leads to less aesthetical pleasure despite the probable sensate skin zone [3, 8]. A type of flap that is taken from the ulnar side of the thumb and based on the dorsoulnar artery of the radial artery is a candidate for thumb defect with advantages such as only one affected finger and early mobilization of the thumb [1]. Free flaps can be used, but this technique requires microsurgical experience, prolonged operation, and a high risk of total flap loss.

The reverse homodigital dorsoradial flap was first described in 1996, based on the dorsal radial collateral artery originating from the radial artery. When the artery goes along the first metacarpal and proximal phalanx on the radial side, about 1 cm from the medial axis of the digit, it finishes at the

middle third of the proximal phalanx by connecting to the palmar circuit to the mobilization of the flap [5, 6]. Regarding the reinnervation on the flap, we didn't decide to coaptation between the branch of the superficial nerve included in the flap and the branch of the digital nerve on the other side. However, we recorded that two - point discrimination was 5 mm after 4 weeks. In the study of Moschella (2006), the author reported that the static two - point discrimination was evaluated only for palmar reconstruction with a mean value of 9.7 mm, which is not very different from the values obtained using techniques of nerve disconnection and reconnection [6].

We conclude that the defects of the hand are caused by traffic, labour, or daily living accidents, and reconstruction has still left the challenges to plastic and reconstructive surgeons to manage in the emergency room and to select suitable flap resurfacing. We used the reverse homodigital dorsoradial island flap for recovering the defects of the thumb and the result is acceptable as expected. However, the data and evidence limitations of the case report can't conclude that it's one of the most appropriate flaps to recover defects of the thumb.

IV. CONCLUSION

The reverse homodigital dorsoradial flap has become a useful and valuable material for thumb reconstruction. The flap provides acceptable aesthetic results with primary closure of the donor site and returns the essential functionality to the affected thumb.

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Case series

EFFICACY AND SAFETY OF THREE - DIMENSIONAL LAPAROSCOPIC ADRENALECTOMY: A SINGLE - CENTER EXPERIENCE

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ABSTRACT

Background: *Laparoscopic adrenalectomy has emerged as the standard treatment for adrenal tumors. Although the application of high - resolution cameras has enhanced visualization in conventional two - dimensional laparoscopy, it has not fully overcome the limitations of depth perception and spatial recognition. However, thanks to significant advancements in three - dimensional technology in laparoscopic surgery, these issues have been totally solved. This study aims to evaluate the outcome of three - dimensional laparoscopic adrenalectomy.*

Methods: *A prospective study included 38 patients with adrenal tumors who underwent three - dimensional laparoscopic adrenalectomy from April 2020 to December 2022 at the Department of Urology, Hue Central Hospital.*

Results: *The mean age was 42.5 ± 5.1 years old. The most common reason for hospitalization was back pain, accounting for 39.5%. Adrenal incidentalomas were detected in 23.7% of patients. The proportion of patients with functional adrenal tumors was 55.3%; nonfunctioning adrenal lesion with progressive growth 13.1% and pheochromocytoma was 7.9%. Computed tomography showed a mean tumor size of 30.5 ± 9.2 mm. The mean operative time was 108.8 ± 12.3 minutes. There were no cases of intraoperative complications or conversion to open surgery. Early postoperative complications include wound infection (5.3%) and fluid accumulation (2.6%). The mean postoperative hospital stay was 5.5 ± 1.9 days. Postoperative pathological reports showed adrenocortical tumors in 81.6%. At follow - up, 35 of 38 (92.1%) cases were asymptomatic and had normal follow - up results in laboratory tests.*

Conclusions: *Three - dimensional laparoscopic adrenalectomy is a minimally invasive, safe, and effective method.*

Keywords: *Adrenal tumor, 3D laparoscopy, laparoscopic adrenalectomy.*

I. INTRODUCTION

The adrenal glands are important endocrine glands that help regulate several bodily functions. In adults, adrenal tumors cause many disorders, they may be hormonally active or nonfunctional as well as malignant or benign. It is important for physicians to determine the characteristics of the lesions and determine the need for any necessary treatment [1, 2]. In 1992, Gagner et al. introduced trans-laparoscopic adrenalectomy with lateral flank access, which has now become the standard approach for adrenal tumor treatment [3]. While high - resolution cameras have improved visualization in standard two - dimensional (2D) laparoscopy, they have not fully addressed the limitations of depth perception and spatial awareness [4]. To overcome these limitations, the development of three - dimensional (3D) technology in laparoscopy provided surgeons with enhanced depth perception, improved identification of anatomical structures, precise manipulation, reduced intraoperative blood loss, and benefits for both experienced and novice surgeons, including shorter operating and training times for residents [4, 5]. Since 2017, 3D laparoscopic surgery has been widely applied in routine clinical practice at Hue Central Hospital. However, there is a lack of studies evaluating the outcomes of 3D laparoscopic surgery in the fields

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of urology, especially adrenalectomy. Therefore, we carried out this study to present our experiences and evaluate the outcomes of laparoscopic adrenalectomy using a 3D system.

II. MATERIALS AND METHODS

2.1. Research subjects

In this study, the selection of research subjects was based on the guidelines provided by the American association of clinical endocrinologists (AACE) and the American Association of Endocrine Surgeons (AAES) in 2009.

Patients were enrolled according to AACE/ AAES guidelines (2009): Hormone - producing adrenal tumors; Pheochromoctoma; Non - functional adrenal tumors or adrenal cysts ≥ 4 cm

Exclusion criteria: Tumors > 7 cm in size; Severe medical diseases that cannot be operated: heart failure, severe renal failure, decompensated cirrhosis, coagulation disorders...

2.2. Methodology

The study was conducted as a prospective study, including patients diagnosed with adrenal tumors who met the selection criteria for 3D laparoscopic adrenalectomy at the Urology Department of Hue Central Hospital, from April 2020 to December 2022.

Parameters:

Pre - operation: Diagnosis of the patient was based on clinical symptoms, adrenal hormone biochemical tests, and computed tomography for tumor imaging evaluation. Patients may present with symptoms such as hypertension, weight gain, or unexplained fatigue. Blood sample analysis is crucial for postoperative hormone assessment and preventing complications following surgery. CT scans allow the surgeon to visualize the structure and size of the adrenal gland and identify any abnormal growths or tumors.

Outcomes: 3D Laparoscopic adrenalectomy was conducted using the transperitoneal approach via the flank in the lateral decubitus position for all patients. Short-term outcomes were evaluated based on operative time, blood loss, transfusion rate, complications, and length of hospital stay. Abdominal drainage was removed on the first postoperative day and postoperative complications were assessed according to the Clavien - Dindo classification. We also compared the mean operative time among different groups based on BMI, tumor location, and tumor size. Surgical outcomes were analyzed and compared with findings from related studies.

Follow - up: Examinations were conducted one and three months after surgery to evaluate symptoms improvement and changes in biochemical tests. In case of post - surgery examinations adrenal biochemical tests show persistent abnormalities, alternative investigation options may be explored.

Statistical analysis: Data analysis was performed using IBM SPSS version 26.0 Software (IBM, Armonk, NY, USA).

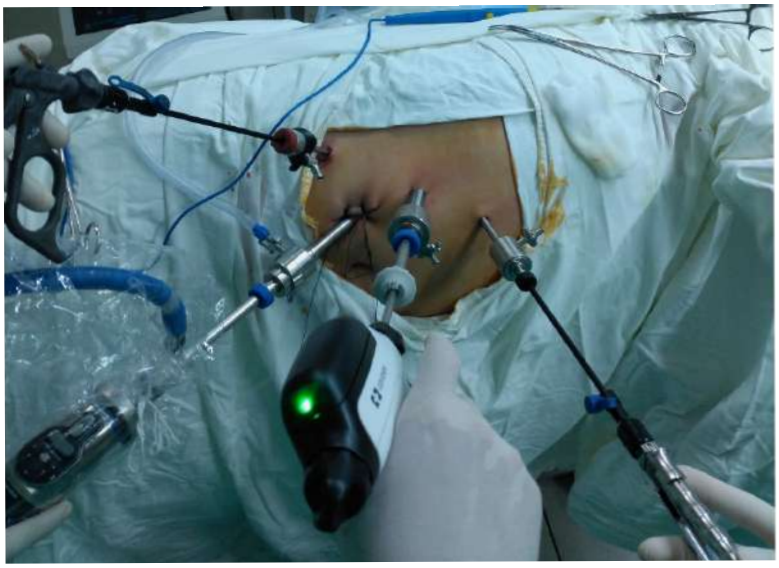

Figure 1: Laparoscopic port placement for right transperitoneal adrenalectomy

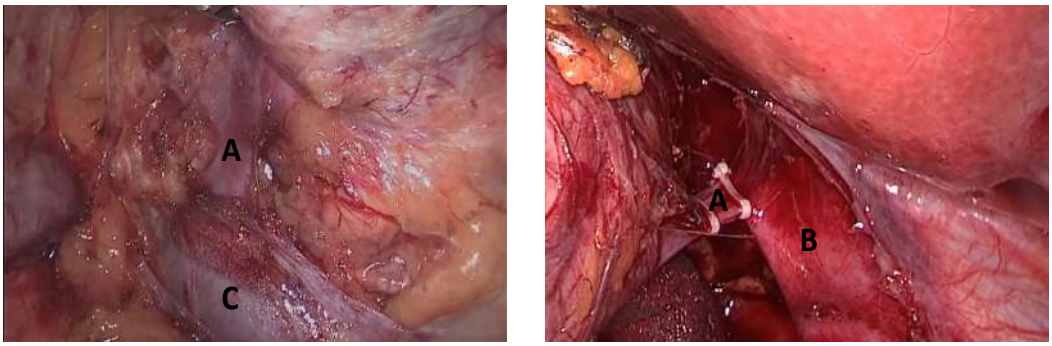

Figure 2: Left: Left adrenalectomy, A: adrenal vein, C: left renal vein
Right: Right adrenalectomy, A: adrenal vein, B: inferior vena cava

III. RESULTS

3.1. Characteristics

Patient demographics and tumor characteristics were shown in Table 1. Our study included 38 patients undergoing 3D laparoscopic adrenalectomy with a mean age of 42.5 years. The majority were male (57.9%). Mean BMI was 22.8 kg/m^2. Tumors were commonly functional (55.3%), right sided (52.6%), and averaged 30.5 mm in size. Hypervascularity was noted in 92.1% of tumors. The most prevalent tumors were cortisol - producing (23.7%), aldosteronomas (31.6%), and pheochromocytomas (7.9%).

Table 1: Characteristics of patient and tumor

Variable	n = 38
Age (years, mean ± SD)	42.5 ± 5.1 (19 - 71)
Gender	
Male	22 (57.9%)
Female	17 (42.1%)
BMI (kg/m^2, mean ± SD)	22.8 ± 4.5 (18.3 - 26.9)
Tumor size (mm, mean ± SD)	30.5 ± 9.2 (10 - 52)
Tumor location	
Right	20 (52.6%)
Left	18 (43.4%)
Vascularity	
Hypervascularity	3 (7.9%)
Normal/ hypovascularity	35 (92.1%)
Incidentaloma	
Adrenal cortical adenoma	6 (15.8%)
Myelolipoma	2 (5.3%)
Neurogenic tumor	1 (2.6%)
Nonfunctioning adrenal lesion with progressive growth	
Adrenal cortical adenoma	4 (10.5%)
Adrenal cyst	1 (2.6%)
Functional adrenal tumors	
Cortisol - producing adrenal tumor	9 (23.7%)
Aldosteronoma	12 (31.6%)
Pheochromocytoma	3 (7.9%)

3.2. Surgical outcomes

The average surgical time was 108.8 minutes. Blood loss was estimated to be 81.5 mL. There were no open surgery conversions. In 7.9% of cases, minor postoperative problems occurred, including wound infections (5.3%) and fluid accumulation (2.6%). The average hospital stay after surgery was 5.5 days. The difference in operating time between BMI and tumor size was substantial (Table 2). Patients with a BMI greater than 23 kg/m^2 required more time during surgery than those with a BMI less than 23 kg/m^2 (115.7 vs 99.1 minutes, p = 0.03). Larger tumors with diameters greater than

40 mm had substantially longer operational times than smaller tumors with diameters less than 40 mm (119.1 vs 95.9 minutes, p = 0.01) (Table 3).

Table 2: Surgical outcomes

	n = 38
Operative time (minute, mean ± SD)	108.8 ± 12.3 (80 - 150)
Estimated blood loss (ml, mean ± SD)	81.5 ± 23.7 (10 - 120)
Conversion No Yes	 38 (100%) -
Postoperative complications No complication Clavien - Dindo I - Wound infection - Fluid accumulation	 35 (92.1%) 3 (7.9%) 2 (5.3%) 1 (2.6%)
Postoperative length of stay (day, mean ± SD)	5.5 ± 1.9 (5-9)

Table 3: Mean operative time among various groups

Variable	**Operative time (mean ± SD)**	**P**
BMI (kg/m²) < 23 ≥ 23	 99.1 ± 10.5 115.7 ± 13.4	 0,03
Tumor location Right Left	 106.3 ± 9.6 109.1 ± 14.8	 0,74
Tumor size (mm) < 40 ≥ 40	 95.9 ± 11.5 119.1 ± 10.0	 0,01

3.3. Postoperative biochemical changes

Preoperatively, abnormalities included included hypokalemia (31.6%), hypercortisolism (23.7%), hyperaldosteronism (18.4%), and increased catecholamines (7.9%). Only 7.9% of patients had mild hypokalemia three months after surgery, although others hormonal hypersecretion was disappeared (Table 4).

Table 4. Plasma biochemical parameters follow-up

Plasma biochemical parameters	**Pre-op**	**Post-op**
↓ Potassium	12 (31.6%)	3 (7.9%)
↑ Aldosterone	7 (18.4%)	-
↑ Cortisol	9 (23.7%)	-
↑ Renin	3 (7.9%)	-
↑ Catecholamine	3 (7.9%)	-

IV. DISCUSSION

According to the AACE/AAES guidelines (2009), incidental adrenal masses that are larger than 4 cm on radiographic images should be surgically removed due to the higher risk of adrenal cancer [6]. Since Garner et al initially described laparoscopic adrenalectomy (LA) in 1992, this procedure has become the standard treatment in patients with small benign adrenal masses [7]. In comparison to open adrenalectomy, laparoscopic adrenalectomy provides better clinical outcomes, lower perioperative morbidity and mortality, a shorter hospital stay, and better cosmetic results.

However, LA has limitations in some groups of patients, including patients with a large adrenal tumor and a high BMI. In our study, the mean duration of the surgery was 108.8 ± 12.3 minutes. Our statistical analysis revealed a correlation between the operative time and the patient's body mass index (BMI) as well as the size of the tumor ($p < 0.05$). Specifically, patients with a BMI greater than 23 kg/m² and a primary tumor size exceeding 40 mm displayed a significant association with a longer operative time.

Notably, our operating time was much lower than Agrusa's study (2016)'s with 120-minute for 2D laparoscopy time and only 10 minutes more than their 110 - minute 3D laparoscopy time [4]. Advanced 3D systems offer superior magnification and stereoscopic viewing of anatomical regions, enhancing the understanding of anatomical structures and facilitating precise tissue dissection and coagulation. Using 3D laparoscopic systems, surgeons gain better control in the operating room and can avoid unintended vascular injuries when

dissecting perivascular adipose tissue [4, 8]. Our estimated blood loss of 81.5 mL was also minimal, further demonstrating the safety of this approach.

No intraoperative complications or transitions to open surgery occurred in our study. Prior to surgical intervention for pheochromocytoma, preoperative diagnosis supports careful dissection and examination of the adrenal veins to minimize excessive tumor manipulation. This approach reduces the risk of excessive catecholamine release and the subsequent development of hypertension. Postoperatively, only minor wound complications occurred in 7.9% of patients and especially no intraoperative complications took place which is lower than intraoperative complication rates of up to 7.7% reported in other studies [4, 8, 9]. The mean hospital stay of 5.5 days was consistent with prior studies [4, 8, 10]. At the 3-month follow-up, nearly all patients had resolution of hormone hypersecretion, similar to other reports demonstrating excellent endocrine outcomes after adrenalectomy. However, no patient experienced acute adrenal insufficiency after surgery. Due to fluid accumulation in the adrenal fossa, the patient was discharged within 4 days after surgery and 6 days after ultrasound scanning.

Table 5. Comparison with other studies

Author	Method	Operative time (min)	Intraoperative complications (%)	Postoperative hospital stays (days)
Our study	3D Lap. Trans.	108.8 ± 12.3 (80 - 150)	0%	5.5 ± 1.9 (5 - 10)
Nguyen Thanh Vinh (2020)	2D Lap. Trans.	80.39 ± 27.72 (35 - 170)	5,2%	5.17 ± 1.35 (3 - 9)
Buono (2019)	2D Lap. Trans.	145 (75 - 240)	6,2%	3,7 (3 - 6)
Agursa (2016)	2D Lap. Trans.	120 (100 - 240)	7,7%	-
	3D Lap. Trans.	110 (100 - 210)	0%	-
Hermosa (2020)	2D Lap. Trans.	98.6 ± 40.8 (30 - 235)	-	3 (1 - 11)
	3D Lap. Trans.	62.6 ± 23.2 (20 - 150)	-	2 (1 - 6)

Lap. - Laparoscopic; Trans. - Transperitoneal

Our results add to the growing body of evidence showing 3D laparoscopy as an effective alternative method to traditional 2D laparoscopic adrenalectomy. The improved depth perception and magnification with 3D imaging may translate to better clinical outcomes and shorter learning curves for surgeons, though further comparative studies are needed. This was only a small case series from a single center, further investigation with a larger patient cohort and a control group is necessary to compare treatment outcomes with the conventional 2D laparoscopic approach. Moreover, the larger multi - institutional studies need to define the advantages of 3D laparoscopic adrenalectomy and long - term oncologic outcomes, patient - reported outcomes, and cost - analyses should be examined as well.

V. CONCLUSION

3D Laparoscopic adrenalectomy is a minimally invasive, safe, and remarkably efficient surgical technique.

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Original research

INITIAL EFFICACY EVALUATION OF ACUPUNCTURE THERAPY FOR POST COVID-19 HEADACHE TREATMENT

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ABSTRACT

Background: *Among all the neurological disorders that can most frequently be found in the post COVID-19, headache symptomatology is a possible chronic sequela of the infection, making up a rate of 19% after 3 months and 16% after 9 months. This study aims to asses the effectiveness and safety of the acupuncture therapy for post COVID-19 headache treatment.*

Methods: *A cross - sectional descriptivestudy was carried out on 40 patients with post COVID-19 headache who were receiving acupuncture treatment at Hue Central Hospital. The primary outcomes were pain VAS (Visual Analog Scale) and HIT-6 (Headache Impact Test). The secondary outcome was adverse therapy reactions.*

Results: *The pain VAS and HIT-6 declined significantly -3.77 ± 1.46 and -15.97 ± 3.25, respectively. No adverse reactions were found during the study.*

Conclusion: *Based on the high quality of evidence, we concluded that acupuncture may be an effective and safe therapy for post COVID-19 headache treatment.*

Keywords: *Post COVID-19 condition, Post COVID-19 headache, Acupuncture.*

I. INTRODUCTION

A new type of coronavirus, called SARS-CoV-2, emerged in China in late 2019 and causes COVID-19. COVID-19 is characterized by respiratory symptoms, including respiratory insufficiency requiring invasive ventilatory support. Since the start of the outbreak in early 2020, other symptoms have been described during the acute stage of infection; these include neurological, gastrointestinal, kidney, and hematological manifestations, among others. Among neurological symptoms, headache is a common complaint [1]. Long COVID refers to the symptoms that last for months after leaving the hospital. These symptoms include easy muscle fatigue, mild shortness of breath, persistent headache, the feeling of a foggy head, and the development of psychiatric disorders. Generally, the life quality of at least half of the people who recover from COVID-19, whether mild or serious, shows a markedly worsening despite having passed a difficult physical and psychological test [2]. According to the World Health Organization (WHO), most people who get COVID-19 recover completely, but there is evidence that around 10–20% of people have different effects that last for a long time after they get better from their initial illness. In October 2022, WHO gave the main official definition of the post COVID-19 syndrome: "Post COVID-19 condition, also known as long COVID, refers to long-term symptoms that some people experience after they have had COVID-19. People who experience post COVID-19 condition sometimes refer to themselves as "long-haulers". These symptoms might persist from their initial illness or develop after their recovery. They can come and go or relapse over time. The most common symptoms of post COVID-19 condition are fatigue, breathlessness and cognitive dysfunction (for

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example, confusion, forgetfulness, or a lack of mental focus or clarity) [3]. Persistent headache is one of the most common neurological problems that can last for a long time after COVID-19. Since this kind of headache does not have a name in the International Headache Society classification, we need to pay attention to this long - COVID-19 headache especially because there are plans to do clinical studies to get big data for the International Headache Society Classification Committee [2]. People who have post COVID-19 condition, also called long COVID, may have trouble functioning in daily life. Their condition may make it hard for them to do everyday activities like work or housework. [3]. Garcia-Azorin D (2022) found that 19.0% of 905 patients had long COVID-19 headache after 3 months and 16.0% after 9 months The severity of headache in the acute phase was linked to a longer duration of headache [4]. The mechanisms causing persistent headache after SARS-CoV-2 infection remain unclear. Clinically, headache in the acute stage is usually holocranial [1]. Despite its high prevalence, the management of this feature remains a challenge and little published proof on the pharmacological treatment of COVID-19 headache is available. Non-steroidal anti-inflammatory drugs (NSAID) might be useful in the acute phase, but this is based on anecdotal evidence [5]. Acupuncture, an important method in Traditional Chinese Medicine, is widely used in clinical practice as a treatment for headache. It is reported that acupuncture was one of the most common complementary therapies in worldwide [6]. To initially initially summarize and evaluate the effectiveness of the acupuncture therapy in the treatment of post COVID-19 headache, we conducted this study to assess the effectiveness and safety of acupuncture for post COVID-19 headache.

II. MATERIALS AND METHODS

2.1. Participants and methods

A cross - sectional descriptivestudy was carried out on 40 patients who were examed and treated as outpatients at Hue Central Hospital, with persistent headache symptoms after COVID-19, who volunteered to participate in the study, from January 2022 to July 2022.

2.2. Study tools and data analysis

Diagnosis criteria: Patients were diagnosed post COVID-19 condition based on WHO definition [2] with persistent headache symptoms.

Inclusion criteria: The inclusion criteria for study patients were as follows: (1) people who have a history of probable or confirmed SARS-CoV-2 infection; (2) usually within three months from the onset of COVID-19, with symptoms and effects that last for at least two months (3)The symptoms and effects of post COVID-19 condition cannot be explained by an alternative diagnosis [2].

Exclusion criteria: Persistent headaches that preceded COVID-19. Primary headache (tensive type headache…) and other secondary headaches such as neurological diseases (traumatic brain injury, hypertension syndrome…). The headache that caused by other bacterial and viral infections (meningitis, encephalitis…), headache caused by chemicals, high blood pressure. Exhaustible body. Pregnancy.

Methods of data collection: clinical examination, performing laboratory tests (complete blood count, blood glucose, urea, creatinine, ALT, AST, CRP, electrocardiogram, EEG, straight chest X-ray, cranial MRI). Participants with no physical lesions on brain MRI and/or CT-scanner continued to be followed up.

Intervention: Patients were treated with acupuncture therapy, following the acupuncture process and acupressure protocol according to the procedure number 15 of the document 26/2008/QD-BYT of the Vietnamese Ministry of Health. Participants received acupuncture treatment 1 times a day, daily for 7 days. Acupressure formula included: GV 20, EX-HN5, EX-HN3, LI 11, LI 4, 2 sides.

We evaluated treatment results 2 times: before the study and 7 days after the intervention (D0 and D7).

Outcome indicators: The primary outcomes were pain VAS (Visual Analog Scale) and HIT-6 (Headache Impact Test). The secondary outcome was adverse therapy reactions. Sociodemographic details including age, sex, body mass index (BMI), history of hospital treatment for COVID-19 disease,

To assess the global impact of episodic headaches in patients consulting general practitioners (GPs) using the Headache Impact Test (HIT-6)

questionnaire, and to compare this with measures of headache severity and quality of life. HIT-6 includes 6 categories: pain, social functioning, role function, vitality, cognitive function, and psychological distress. The patient answered 6 questions with a choice of 1 of 5 answers "never", "rarely", "sometimes", "frequently" and "always". Combined with the multiplier formula for each answer item, the total score ranges from 36 - 78 [7].

The Visual Analogue Scale (VAS) measures pain intensity. The VAS consists of a 10 cm line, with two end points representing 0 ('no pain') and 10 ('pain as bad as it could possibly be').

Ask the patient to rate their current level of pain by placing a mark on the line. Use a ruler to measure the distance in centimetres from the 'no pain marker' (or zero) to the current pain mark. This provides a pain intensity score out of 10.

Data were collected by questionnaire, interview, and medical records. Statistical analysis was performed with the use of Microsoft Excel 2016 and Statistical Product and Services Solutions SPSS 20.0.

All information was only used for scientific purposes.

III. RESULTS

3.1. Study characteristics

Table 1 figured the sociodemographic details of the patients who recovered from COVID-19 infection, including age, sex, Body Mass Index (BMI), history of hospital treatment for COVID-19 disease.

Table 1: Baseline characteristics

Characteristics		n	Percentage (%)
Age	$\overline{X}$ ± SD	41.35 ± 14,43	
Sex	Male	17	42.5
	Female	23	57.5
Body Mass Index	$\overline{X}$ ± SD	22.71 ± 5.26	
History of hospital treatment for COVID-19 disease	Yes	22	55
	No	18	45

The mean of age was 41.35 ± 14.43. The majority of participants was female (57.5%). The BMI mean score was 22.71 ± 5.26. Most of participants had a history of hospital treatment for COVID-19 disease.

Table 2. Illustrated the ratio of other post COVID-19 symptoms.

Symptoms	n	Percentage (%)
Fatigue	34	85
Shortness of breath or difficulty breathing	17	42.5
Memory, concentration problems	8	20
Sleep disorder	13	32.5
Chest pain	11	27.5
Persistent cough	10	25
Muscle aches	5	12.5
Loss of smell or taste	3	7.5

The commonly symptoms of post COVID-19 condition were fatique (85%), shortness of breath or difficulty breathing and headache (42.5%), sleep disorder (32.5%). The other symptoms are memory and concentration problems (20%), persistent cough (25%), muscle aches (12.5%) and loss of smell or taste (7.5%).

3.2. Treatment results

Table 3 illustated the evaluation of the effectiveness of treatment for post COVID-19 headache based on VAS score.

Table 3: VAS score after treatment

Time	VAS score ($\overline{X}$ ± SD)
D_0	6.05 ± 1.29
D_7	2.27 ± 1.3
Reduction	-3.77 ± 1.46
$p_{(7-0)}$	< 0.01

Before and after treatment, The VAS scores were 6.05 ± 1.29 and 2.27 ± 1.3 ($p < 0.01$). The VAS reduction was -5.43 ± 3.51.

Table 4: Post COVID-19 headache treatment according to HIT-6 score

Time	HIT score ($\overline{X}$ ± SD)
D_0	61.95 ± 5.95
D_7	45.75 ± 6.71
Reduction	-15.97 ± 3.25
$p_{(7-0)}$	< 0.01

The HIT-6 scores were 61.95 ± 5.95 at D0 and 45.75 ± 6.71 at D7 (< 0,01). The decrease in HIT-6 score was -15.97 ± 3.25.

No adverse drug reactions were found during the treatment, including diarrhea, dizziness, fatigue, dry mouth, bloating, constipation, tachycardia, blurred vision, tremor and anorexia.

IV. DISCUSSION

The mean age was 41.35 ± 14,43. The majority of patients were female (57.5%). The mean score of BMI was 22.71 ± 5.26. The rate of hospital treatment history for COVID-19 disease accounted for 55%. The most common symptoms of post COVID-19 condition were fatigue (85%), shortness of breath or difficulty breathing and headache (42.5%), sleep disorder (32.5%). This study results were similar to the other survey and reports [8 - 9]. In B. Oronsky's report, the two most common central nervous system symptoms were dizziness (16.8%) and headache (13.1%) [8]. A. Pavli's research illustrated that common symptoms are fatigue (85%), residual dyspnea (10 - 40%), mental problems (26%), chest pain (22%), olfactory and gustatory dysfunction (11%) [9]. After having COVID-19, most people get better, but some people have mid - and long - term effects that last for a while. Post COVID-19 condition, or "long COVID," is the term for the group of long - term symptoms that some people have after COVID-19. People who have post COVID-19 condition sometimes call themselves "long - haulers". Some people have mid - and long - term effects like fatigue, breathlessness and cognitive dysfunction (for example, confusion, forgetfulness, or a lack of mental focus and clarity). Some people also suffer psychological effects as part of post COVID-19 condition. These symptoms might carry on from their initial illness or develop after their recovery. They can come and go or relapse over time. Post COVID-19 condition can make it hard for a person to do everyday things like work or chores. Symptoms are different for different people, and for adults and children. The most common symptoms of post COVID-19 condition include: fatigue, shortness of breath or difficulty breathing, memory, concentration or sleep problems, persistent cough, chest pain, trouble speaking, muscle aches, loss of smell or taste, depression or anxiety and fever [3].

Persistent post - COVID-19 syndrome, also referred to as long COVID-19, is a pathologic entity, which contains persistent physical, medical, and cognitive sequelae following COVID-19, including persistent immunosuppression as well as pulmonary, cardiac, and vascular fibrosis [3].

Pathologic fibrosis of organs and vasculature causes to increased mortality and severely worsened quality of life. Inhibiting transforming growth factor beta (TGF-β), an immuno - and a fibrosis modulator, might help with these post - COVID problems. Current preclinical and clinical efforts are focused on the mechanisms and manifestations of COVID-19 and its presymptomatic and prodromal periods; by comparison, the postdrome, which occurs in the aftermath of COVID-19, which we refer to as persistent post - COVID - syndrome, has received little attention. The long - term effects of post - COVID syndrome will become more important as more treated patients leave the hospital, putting pressure on healthcare systems, patients' families, and society in general to take care of these COVID-19 survivors who have serious medical problems [8].

The reduction of VAS and HIT-6 scores were -5.43 ± 3.51 and -15.97 ± 3.25, respectively. 40 participants who received acupuncture treatment for 7 days, reported no specific adverse reactions. None of the patients experienced any adverse drug reactions from the treatment, including diarrhea, dizziness, fatigue, dry mouth, bloating, constipation, tachycardia, blurred vision, tremor and anorexia.

Clinical research of A.V.Krymchantowski on 37 patients showed that patients took indomethacin orally at a dose of 50 mg two times a day and pantoprazole 40 mg once a day, for 5 days. On the third and fifth days of the treatment, they used

a headache diary to measure the frequency and intensity of their headache. They classified the pain intensity using a visual analog scale (VAS) as VAS 1 - 4 (mild), VAS 5 - 7 (moderate), VAS 8 - 9 (severe), and VAS 10 (very severe). After treatment with indomethacin, 36 patients reported greater than 50% headache relief from the third day and 5 became asymptomatic on the fifth day. For 5 days, [5]. Treating headache in COVID-19 patients may be difficult. No consensus exists on the medications for this particular type of headache and various drugs have been experimented with anecdotal outcomes. A case report described a chronic migraine patient with COVID-19 comorbidities who was already using fremanezumab and had a resistant headache. She tried many drugs and then received lacosamide IV and other drugs that seemed to improve her condition. Non-steroidal anti-inflammatory drugs were initially contraindicated for COVID-19 patients by the World Health Organization (WHO), but the recommendation was later reversed [5].

Headache occurs as one of the initial symptoms of infection in COVID-19. It can spread over the head, making it feel constricted and heavy. This happens in a large part of people who have the first signs of COVID-19, from 14 to 60%. The so - called long COVID is the group of symptoms that stay with the patient for months after they leave the hospital [8]. These symptoms include muscle fatigue, moderate breathlessness, persistent headache, the feeling of a foggy head, and the development of psychiatric disorders. In general, the quality of life of at least half of the patients who recover from COVID-19, both mild and severe, shows a markedly worsening despite having passed a difficult physical and psychological test. The neurological impairment of post-COVID-19 could have different pathophysiological bases: direct neuro-invasion with a damage on the neuronal pathway, indirect effects mediated by hypoxia, hypertension, coagulopathy and cytokine storm on the central nervous system, up to the worsening of pre - existing brain diseases or new ones (cerebrovascular events, infections, toxic encephalopathy, meningoencephalitis and Guillain Barré syndrome) [8]. Long - term problems come from this complex picture. Among all the neurological disorders that can most frequently be found in the "long COVID-19," it is not necessary to underestimate the persistent headache for at least 6 months, both as a sign of new onset along with cognitive dullness, like "brain fog," and as worsening/making chronic a migraine that was already there. Even though headache is not a sign of how COVID-19 will progress, it should always be considered as a possible long-lasting effect of the infection. A similar clinical picture of ongoing headache was already seen, as a result of other viral infections, as the New Daily Persistent Headache (NDPH), and was reported by Diaz-Mitoma and Walter Vanast of McGill University in Montreal, as headache caused by Esptein-Barr Virus infection and published in 1987 in Lancet, headache syndrome that lasts > 3 months. However, this putative similarity between NDPH and long - COVID-19 headache needs further discussion and data [8]. The presence of this complex neurological symptomatology, headache and foggy feeling, even after negativization by COVID-19 infection, must be taken seriously in order to prevent a chronicity of the headache and a further decline of the patient's quality of life. Moreover, abnormal innate immune signaling and activation of inflammasomes involved in both COVID-19 headache and migraine, could also have a role in long - COVID headache, as well as sleep problems associated with long - COVID symptoms also be a significant factor causing cognitive problems, poor memory, and chronicity of headaches [8]. According to Traditional Medicine, the headache belongs to the original disease, located in the debilitating mental illness that causes the feeling of foreign evil or dysfunction in the functioning of the government. Healing with acupuncture is a long-standing legacy in oriental medicine. The purpose of acupuncture is to "regulate the qi", to create a stimulus into the acupoint to create a Yin - Yang balance, that is, to restore the physiological state, eliminate the pathological state, and bring the muscles back to work. movement of normal function. Treatments for the post - COVID-19 syndrome, with its long-lasting symptoms, are still being researched and debated. The pain VAS is an unidimensional measure of pain intensity, used to record patients' pain progression, or compare pain severity between

patients with similar conditions. HIT-6 test includes 6 categories: pain, social functioning, role function, vitality, cognitive function, and psychological distress. Characteristics of changes in pain VAS and HIT-6 scores mean improvement in pain, severity of headache and improvement in patient's quality of life before and after intervention. The therapeutic effect of acupuncture on other symptoms of post - Covid-19 syndrome continues to be researched, such as sleep disorder, chest pain, loss of smell or taste. Acupuncture is an alternative and additional treatment, with few side effects, as one of the treatment options in clinical.

Currently, the evidence and recommendations in the treatment of this syndrome, especially the post-COVID-19 headache, have not yet been reported. Against statistical purposes, evaluate and contribute to research in the treatment of the post - COVID-19 syndrome developed at the unit, together with the employer of the Ministry of Health and the hospital in the treatment of the post - COVID-19 syndrome-19, we have been conducting research and evaluation on this issue since January 2022.

V. CONCLUSION

Based on the high quality of evidence, we concluded that acupuncture may be an effective and safe therapy for post COVID-19 headache treatment.

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Original research

ASSESSMENT OF PULMONARY VASCULAR RESISTANCE VIA DOPPLER ECHOCARDIOGRAPHY IN ISCHEMIC HEART DISEASE WITH REDUCED EJECTION FRACTION

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ABSTRACT

Objectives: *To determine pulmonary vascular resistance (PVR) by echocardiography - Doppler; and evaluate the correlation between pulmonary vascular resistance and some variables such as left ventricular EF, PASP, TAPSE, and tissue S-wave of the tricuspid valve in patients with ischemic heart disease.*

Method: *Observational study on 82 heart failure patients with reduce ejection fraction brought upon by ischemic heart disease, at the Cardiology Department of the University of Medicine and Pharmacy from 04/2016 - 05/2017.*

Results: *The average PVR is 3.91 ± 1.85 WU. There was not significant difference between age and gender groups ($p > 0.05$), but there was a statistically significant difference of PVR in patients with NYHA III and IV compared to NYHA I, II ($p < 0.05$). When EF < 30%, the rate of increased PVR is higher than the normal value (35.4 % vs 4.9%). There is a strong correlation between LVEF and PVR ($r = - 0.545$, $p < 0.001$), especially when PVR < 8 WU ($r = - 0.618$, $p < 0.001$). When the PASP increases, the rate of increased PVR is higher than normal value (54.9% vs. 9.8%, $p < 0.001$), with an enough correlation coefficient ($r = 0.361$, $p < 0.001$). In patients with RV systolic dysfunction evaluated by TAPSE and S' wave, there was a significant difference in the rate of increased PVR from the normal value (41.5% vs 1.2%; 34.1 vs 8.5%, p 0.001). PVR is closely correlated with TAPSE ($r = -0.590$; $p < 0.001$) and is inversely correlated with S' wave ($r = -0.590$; $p < 0.001$).*

Conclusions: *Increased PVR is the primary mechanism for pulmonary hypertension and right ventricular dysfunction in patients with HFrEF brought upon by IHD. The evaluation of PVR in patients with left ventricular dysfunction by echocardiography is important in clinical practice.*

Keywords: *Pulmonary vascular resistance, echocardiography, heart failure, reduced ejection fraction.*

I. INTRODUCTION

To balance the afterload of the heart, the connection of the right ventricle (RV) and pulmonary circulation plays an important role. The left ventricle (LV) partially transmits the forces to the RV through the interventricular septum. Therefore, the synchronous contraction and relaxation of LV and RV were achieved. When the LV failure occurs, the RV afterload is gradually increased due to post-capillary pulmonary artery hypertension (PAH) which translates into elevated pulmonary vascular resistance (PVR) [1].

Ischemic heart disease (IHD) is a consequence of myocardial oxygen supply and demand imbalances, caused by coronary atherosclerosis [2]. The long-term effect is heart failure. Heart failure with reduced ejection fraction (HFrEF) increases when the left ventricular ejection fraction (LVEF) is below 40%. When LV failure progresses, the RV function will be affected via multiple mechanisms in which increased

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PVR plays a vital role [3 - 6]. Recent studies suggest that increased PVR, pulmonary hypertension, and RV systolic dysfunction are independent factors for poor prognosis in patients with LV failure [6 - 8].

Cardiac catheterization is the gold standard of the PVR evaluation, but its use is limited by its invasive nature and certain risks. Using echocardiography helps to evaluate RV function, PASP and PVR, which is the most reliable, non-invasive technique [9].

We aim to engage our comprehension of PVR in patients with HFrEF brought upon by IHD, we conducted this study to determine PVR by using echocardiography - Doppler in HFrEF brought upon by IHD; and evaluate the correlation between PVR and some variables such as LVEF, PASP, TAPSE, and tissue S-wave of the tricuspid valve (S') in these population.

II. METHODS

2.1. Study population

We enrolled 82 patients with HFrEF (LVEF < 40%) brought upon by IHD at the Cardiology Department of the University of Medicine and Pharmacy from 04/2016 - 05/2017. IHD also called coronary heart disease (CHD) diagnosed with the significant stenosis of denovo coronary arteries or with documented (prior) MI or coronary artery revascularization (either with PCI or CABG) [2, 9]. Patients with congenital heart disease, primary pulmonary hypertension, or non-IHD diseases lead to pulmonary hypertension were excluded from the study.

2.2. Methodology

Observational Study was performed. All patients underwent investigations and evaluate the cardiovascular risk factors [10]. Doppler echocardiography (EnVisor CHD; Philips, USA) was performed after enrollment. All data of echocardiography were collected [11]:

+ Evaluating the structure and measuring routine echocardiogram parameters.

+ LVEF measured by Simpson method.

+ RV systolic function is assessed by using tissue S-wave of the tricuspid valve (S'), and TAPSE index. TAPSE is defined as the distance traveled between end-diastole and end-systole at the lateral corner of the tricuspid annulus. TAPSE has been validated to correlate strongly with RVEF measured by radionuclide angiography, with low observer variabilities [9].

+ Pulmonary artery systolic pressure (PASP) was calculated by tricuspid regurgitation peak velocity (TRV peak) and right atrial pressure.

+ PVR was calculated by tricuspid regurgitation velocity (TRV) and the time-velocity integral of the RV outflow tract (VTIRVOT) according to the Arm E. Abbas formula. A cutoff value for the Doppler equation was generated to determine PVR >2 Wood units (WU) [12].

Table 1: Important parameters of echocardiography

HFrEF: LVEF < 40%
Normal TAPSE value: ≥ 16mm
Normal S' value: ≥ 9 cm/s
PASP = 4 (TRV)2 + RA pressure
PVR = (Vmax of TR / VTIRVOT) x 10 + 0.16

2.3. Statistical analysis

SPSS 20.0 was used for data analysis. Variables described by rate, mean value ± standard deviation. Regression analysis was used to determine the correlation between PVR and LVEF, PASP, TAPSE, and S' wave. The significance level is 0.05, and the corresponding confidence level is 95%.

III. RESULT

3.1. Baseline characteristics

Most patients had at least one cardiovascular disease risk factors: HBP, smoking and diabetes mellitus (DM). The mean age was 74.1 ± 10.9, with 46 males. There was 43.9% of patients hospitalized with NYHA class III and IV.

Table 2: Clinical characteristics

Parameters	n (%)
Age	
Mean	74.1 ± 10.9
Min	42
Max	93
Age > 70 (%)	70.1
Gender (M/F)	46/36
Hypertension	47 (57.3)
Smoking	41 (50.0)
Diabetes	12 (14.6)

Parameters	n (%)
NYHA (%)	
I	8.5
II	47.6
III	28.0
IV	15.9
CCS (%)	
I	25.6
II	31.7
III	26.8
IV	13.4

The table 2 showed mean of LDL-Cholesterol was 2,77 ± 0,91 µmol/l. The mean of LVEF was 31.5 ± 5.4%. LV regional wall motion abnormalities were found in the majority of patients (70.7% of hypokinesia; 53.7% of akinesia). There was 42.7% of RV systolic dysfunction according to TAPSE, 42.7% of RV systolic dysfunction according to S' waves. The increased of PASP was 72%.

Table 3: Paraclinical characteristics

Parameters	Value	Parameters	Value
LDL-Cholesterol (µmol/l)(Mean)	2.77 ± 0.91	Echocardiography LVEF (Simpson, %) (Mean)	31.5 ± 5.4 (Rate,%)
ECG (Rate, %)		Hypokinesia	70.7
Arrhythmia	35.4	Akinesia	53.7
ST-T changes	65.9	Decreased TAPSE	42.7
Necrosis Q	75.4	Decreased S'	42.7
Pathological T wave	98.8	Increased PASP	72.0

3.2. Pulmonary vascular resistance

The mean PVR was 3.91 ± 1.85 WU. There was not statistical difference between age and gender groups (p > 0.05). There was 35.4% of cases had normal PVR (35.4%). increased PVR (43.9%) prevails, compared to the group with moderate or severe PVR elevation (p < 0.001).

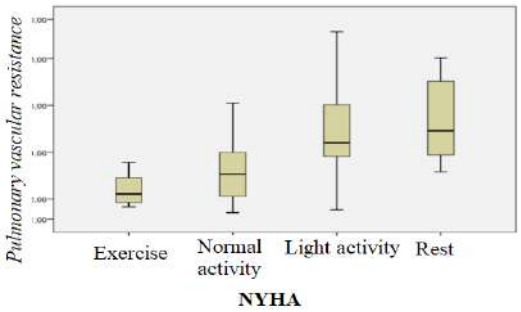

Figure 1: Comparison of mean PVR values by NYHA groups

In the NYHA III/IV group, the proportion of patients with elevated PVR was higher than the normal PVR value (p < 0.001). The mean PVR increased gradually from NYHA group I to group NYHA IV (p < 0.001) (p < 0.001). In the HFrEF group, the rate of increased PVR is 35.4% compared to 4.9% for normal PVR (p < 0.001). Patients with both elevated PVR and elevated PASP had the highest incidence (54.9%).

Table 4: The rate of increased PVR follows LVEF, TAPSE, S' wave, and PASP

	Increased PVR, n (%)	Normal PVR, n (%)	Total, n (%)	p
EF				
< 30%	29 (35.4)	4 (4.9)	33 (40.2)	
> 30%	24 (29.3)	25 (30.5)	49 (59.8)	< 0.001
Total	53 (64.6)	29 (35.4)	82 (100.0)	

	Increased PVR, n (%)	Normal PVR, n (%)	Total, n (%)	p
S’				
Decreased	28 (34.1)	7 (8.5)	35 (42.7)	< 0.001
Normal	25 (30.5)	22 (26.8)	47 (57.3)	
Total	53 (64.6)	29 (35.4)	82 (100)	
TAPSE				
Decreased	34 (41.5)	1 (1.2)	35 (42.7)	< 0,001
Normal	19 (23.2)	28 (34.1)	47 (57.3)	
Total	53 (64.6)	29 (35.4)	82 (100)	
PASP				
Increased	45 (54.9)	14 (17.1)	59 (72.0)	< 0,001
Normal	8 (9.8)	15 (18.3)	23 (28.0)	
Total	53 (64.6)	29 (35.4)	82 (100)	

There was 54.9% of cases had increased PVR and increased PASP, while only 9.8% of cases had increased PVR only ($p < 0.001$). The percentage of patients with both increased PVR and RV systolic dysfunction as determined by the TAPSE index were 41.5% and by the S’ wave was 34.1% ($p < 0.001$).

3.3. Correlation of PVR with LVEF, PASP, S’ wave, and TAPSE index

There was a strong correlation between the PVR and LVEF ($r = - 0.545$, $p < 0.001$), according to the regression equation: $Y = - 0.187X + 9.281$. When PVR < 8 WU, this correlation was stronger ($r = - 0.618$, $p < 0.001$), according to the regression equation: $Y = - 0.171X + 9.079$. There was a moderate positive correlation between PVR and PASP ($r = 0.361$; $p = 0.001$), according to the regression equation: $Y = 0.049X + 2.084$. There was a strong negative correlation between PVR and TAPSE ($r = -0.590$; $p < 0.001$), according to the regression equation: $Y = - 0.249X + 8.237$. There was a moderate negative correlation between PVR and S’ wave ($r = - 0.402$; $p <0.001$), according to the regression equation: $Y = - 0.283X + 6.659$

IV. DISSCUSSION

We enrolled 82 HFrEF patient throught by upon IHD with high risk of cardiovascular risk factor. RV systolic dysfunction might develop in association with LV dysfunction via multiple mechanisms [8]. Bursi et al showed that the percentage of PASP was 79% [13]. In the study of C. Jaarsmar et al, there was a correlation between LVEF and TAPSE measured by cardiac MRI ($r = 0.50$, $p < 0.001$) [14]. Our study results was similar to those of previous studies.

In the NYHA III/IV group, the rate of increased PVR was much higher than in the other group ($p < 0.001$). In terms of pathogenesis, increased PVR was a consequence of pulmonary vascular remodeling, which was an important link in the progression to “reactive” pulmonary hypertension in patients with left heart disease, which in turn causes dyspnea on exertion [8]. When we analyzed the degree of heart failure, we also found a high incidence of increased PVR in the EF < 30% group (54.9%). This result was similar when compared to the study of Fabregat-Andrés et al. [15].

Our study found that the rate of patients with both increased PVR and RV systolic dysfunction was 75.6% (41.5% assessed by TAPSE and 34.1% assessed by S’ wave), compared to 54.9% in the presence of elevated PASP. The increased PVR and RV systolic dysfunction are two important factors in the progression of LV systolic failure. Pham Thi Tuyet Nga (2013) [4] showed an increased PVR in majority of patients. Nguyen Thi Mai Ngoc (2012) [3] studied patients before atrial septal defect closure, and the results showed that the average PVR was 2.25 ± 1.31 WU compared to a control group of 1.31 ± 0.20 WU.

In our study, PVR was closely correlated with LVEF ($r = -0.545$; $p < 0.001$), especially when SCMP < 8 ($r = - 0.618$; $p < 0.001$). This result was similar to that of Garcia-Alvarez et al. [15]. M Assadpour Piranfar showed the mean PVR decreased, corresponding to LVEF ($p = 0.004$) [16].

Increased PVR causes pulmonary artery hypertension. It is therefore not surprising that PVR

and PASP are correlated. With the results obtained, we affirm once again this correlation with r = 0.361 and p = 0.001, lower than authors Nguyen Tan Vuong [5] with r = 0.55 and Pham Thi Tuyet Nga [4] with r = 0.65. The population selection of Nguyen Tan Vuong and Tran Thi Tuyet Nga enrolled both valvular heart disease and congenital heart disease. The prolongation period of progress pulmonary vascular remodeling in congenital heart diseases was clearly longer than in IHD, so PVR would be higher.

With the RV systolic function, we found a strong positive correlation of PVR and TAPSE (r = - 0.590, p < 0.001) and a moderate negative correlation with S' waves (r = -0.402, p < 0.001). In study of M Assadpour Piranfar, the average PVR decreased as TAPSE increased and vice versa to the 18mm TAPSE cutoff point (p = 0.026) [16].

V. CONCLUSION

PVR by using echocardiography is a crucial index that helps early recognition of RV systolic dysfunction secondary to HFrEF throught by upon IHD as well as treating patients and possibly reversing the clinical manifestations effectively and improving prognosis.

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Case report

CLINICAL USE OF CLEAR ALIGNER IN CLASS I MALOCCLUSION

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ABSTRACT

Orthodontics is one of the increasingly popular dental specialties. With the driving force in technology and the development of materials, nowadays, straightening options is more predictable with clear aligner, it helps to improve the problems of malocclusion more possibly and more comfortably. It is known as a highly aesthetic orthodontic appliance, which is near-invisible, enhances oral hygiene as well as comfort during treatment. Invisalign is one of the pioneers in clear aligners, that's why clear aligners is warmly welcomed all over the world and particularly in Vietnam. In this article, we report two cases of comprehensive treatment with clear aligner from Invisalign within 18 months, under the support of artificial intelligence to plan tooth movement through Clincheck© software. The aim is to present the efficacy of the latest orthodontic therapy, and to offer patients more treatment options in correcting various types of malocclusion.

Keywords: *Clear aligners, Invisalign®, orthodontic treatment, malocclusion.*

I. INTRODUCTION

Orthodontic treatment has become a trend in recent decades to enhance the appearance of the smile and to offer consequence regarding patients' oral health. The effectiveness of orthodontic treatment with fixed appliances has been well-established for many years, associated with the image of the braces system. However, with aesthetic requirements in mind, scientists are always looking for ways to improve materials and force generation methods to meet the increasing demands from patients. The arrival of new and more aesthetically pleasing options in orthodontic treatment, such as lingual braces and clear aligners (CA), offers a more convenient experience for both patients and professionals. Among that, CA therapy has clearly become a potential treatment option for patients, especially adults, who require orthodontic treatment that will not have a detrimental effect on their social and personal lives [1]. In the Vietnamese market, this form is still relatively new with high cost of use.

According to reports, the first tray for the idea of using an elastic and removable tooth positioning appliance in orthodontic treatment was born in 1945 [2]. Personalized by the dentist from the patient's periodic dental impressions. By time, scientists have created many artificial materials with advanced properties to increase the efficiency of tooth movement and reduce the number of visits as well as the time chair.

In 1997, CA were invented by a student named Zia Chishti. This CA was later commercialized by Align company (Align Technology, Inc, Santa Clara, California, USA), under the name Invisalign clear aligner, using software technology developed for treatment diagnosis, simulation and fabrication. With the nature of clear sequential removable thermoplastic appliances [3], when placed CA in the mouth, the orthodontic tray will generate a small amount of optimal force to aid in moving the teeth to a new position. By changing the tray sequentially, the teeth will gradually move towards the desired position. So, CA touch the need of the patient is not only because of its flexible disassembly and high aesthetics, but also the virtual technology that simulates the tooth movement with the support of artificial intelligence (ClinCheck© software - exclusive to Invisalign), it shows the process of

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tooth movement and simulated the final outcome. CA allows for a wide range of treatment options, from class I to class II, III malocclusion, from mild to moderate crowding, tooth spacing, cases with extraction premolar as well as case combined with surgery. Time by time, this appliance is widely indicated and recognized as the most aesthetically effective option for tooth movement. Each company distributing orthodontic trays will have its own data collection system, Invisalign® acquires 3D digitized denture data through a CAD-CAM system by using an intraoral scanner (named iTero), then ClinCheck© use the collected data to analyze and to show a virtual outcome simulation, after that, 3D printing technology with thermoplastic ink was used to print a series of treatment trays [4]. Patients must wear the trays according to the recommended order and time (20-22 hours per day, 10-14 days per tray).

As a role of pioneer with lots of years experience, product of Invisalign® becomes a new and potential dental treatment appliance to meet the needs of patients. This report describes two cases of comprehensive treatment with CA from Invisalign® within 18 months.

II. CASE PRESENTATION

Case 1:

A 26-year-old woman, working as an editor of VTV8 television channel, presented with a Class I malocclusion and maxillary anterior crowding. As her job requires high quality facial aesthetic, she would like to undergo her orthodontic treatment with CA instead of traditional system of fixed appliances (wires, elastic tie and brackets).

Examination: She was in the permanent dentition with class I of first molar, moderate crowding in the maxilla (#5mm), especially upper canines located outside the arch and mild crowding in the mandibular (#2mm), moderate overjet (#3mm) and overbite (#2.7mm) (Figure 2). Her primary concern was the alignment of her maxillary incisors and she refused to fix appliances.

The treatment objectives using Invisalign® were to align her upper anterior incisors and alleviate crowding in both jaws (see treatment outcome simulation in Figure 2.D). The occlusal goals were to maintain class I of molar and obtain class I of canines, keep a normal overbite and overjet and achieve a functional occlusion.

The first treatment with Invisalign® involved 38 upper and 21 lower aligners. Attachments were placed on almost teeth to achieve a more predictable tooth movement using aligners. The patient was instructed to change the aligners every 10 days and to wear the tray for at least 22 hours per day. She was required to have a follow-up examination every 3 months or when it is time to interproximal reduction (IPR) on Teeth, according to the staging of movement. After 9 months, at the time of follow-up examination, the patient was wearing tray number 27, the tray was noted to not fit tightly (off tray) at both upper canines, they have not reached the position predicted by the ClinCheck©. The doctor changed the treatment plan to increase more direction of force on upper canines. The second of Invisalign® treatment presented 18 upper and 8 lower aligners. The patient was required to use elastic from the position of the hook cut on upper canines to the button on lower molar to increase the extrusion force. When the treatment was completed, a bonded lingual fixed retainer was placed on the upper and lower incisors to prevent relapse. For retention, the patient was given a Hawley wrap around for both arch and an Essix retainer. The patient was instructed to use the removable appliances full time for 6 months and nighttime thereafter.

Figure 1: Patient's profile (before treatment) - case 01

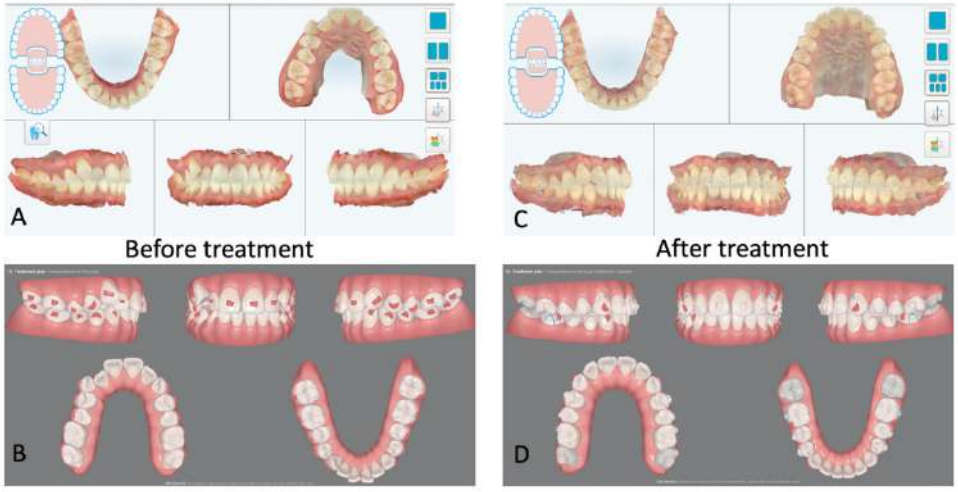

Figure 2: Photo taken by iTero - intraoral scanner (before and after treatment): Images of dental arch and occlusion (A&C), Simulated images recorded by Clincheck© (B&D)

Figure 3: Patient's profile (after treatment) - case 01

Case 2:

A 28-year-old woman, working as a customer care specialist of a life insurance company, presented with a Class I malocclusion and maxillary anterior spacing. Not only the need to communicate with her customers every day was a big problem, but also she had a difficult to schedule her regular dental appointments, so she would like to choose CA for her orthodontic treatment.

Examination: She was in the permanent dentition with class I of first molar and canines, four wisdom teeth are present on the jaw, moderate spacing in the maxillary (#3mm), moderate overjet (#2.5mm) and overbite (#1.8mm). Her primary concern was close all the space in the maxillary, especially maxillary incisors and she deny to use fixed appliances.

The treatment objectives using Invisalign® were to close all the space in the maxillary (see treatment outcome simulation in Figure 4.D). The occlusal goals were to maintain the Class I of molar and canines, keep a normal overbite and overjet and achieve a functional occlusion.

The first treatment with Invisalign® involved 20 upper and 20 lower aligners. Attachments were placed on almost teeth to achieve a more predictable tooth movement using aligners. The patient was required to use elastic from the position of the hook cut on lower canines to the button on upper molar. The patient was instructed to change the aligners every 10 days and to wear the tray for at least 22 hours per day. Patient was required to have a follow-up examination every 3 months or when it is time to interproximal reduction (IPR) on Teeth, according to the staging of movement. After 7 months of initial treatment, a case refinement with 20 more aligners was needed to finish the maxillary arch, and time of changing the aligners is for every 7 days. Once treatment was completed, a bonded lingual fixed retainer was placed on the upper and lower incisors to prevent relapse. For retention, the patient was given a Hawley wrap around for both arch and an Essix retainer. The patient was instructed to use the removable appliances full time for 6 months and nighttime thereafter.

Figure 4: Patient's profile (before treatment) - case 02

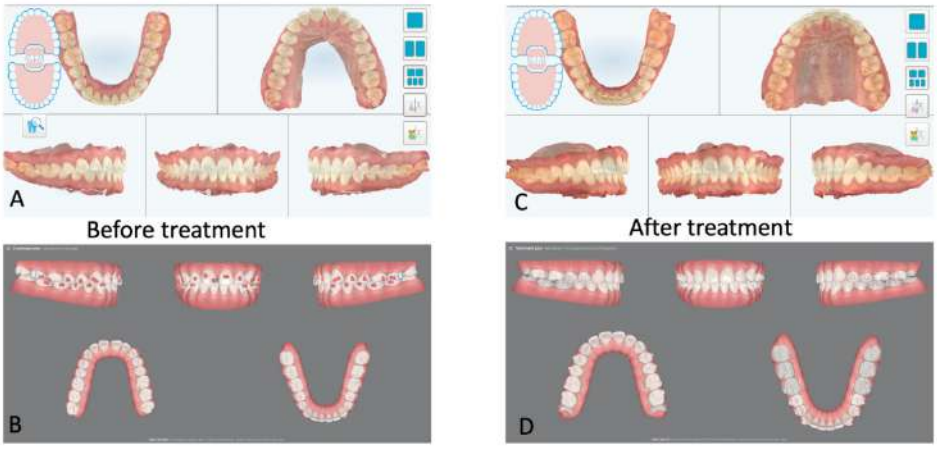

Figure 5: Photo taken by iTero - intraoral scanner (before and after treatment):
Images of dental arch and occlusion (A&C), Simulated images recorded by Clincheck© (B&D)

Figure 6: Patient's profile (after treatment) - case 02

III. DISCUSSION

Some authors have questioned whether the results obtained over the course of treatment with aligners were the same as the AI's simulation in ClinCheck©, however there are currently no studies which are strong enough to answer [5]. But, observations on the treatment results of the two cases in this report show that virtual images are approximately the same as the patient's final occlusion.

The CA has demonstrated results in anterior alignment and good improvement in occlusion, jaw expansion (without surgery), overjet and overbite correction. Also, it can perfectly adjust the midline [6]. CA can be quite effective in reducing deep bites and mild crossbites [4]. With continuous improvement in technique and materials, the benefits of CA are increasing, such as reducing chair's time, increasing the comfort of wearing, easier to clean and more aesthetically pleasing [7, 8].

Compared with conventional removable or fixed appliances, CA combine perfectly with crown anatomy and thus possess the ability of three-dimensional, more controlled movement of the teeth [9]. Furthermore, aligner thickness could provide adequate vertical clearance for cross-bite correction (if present), avoiding use to much additional appliance supporting. CA can also

prevent aesthetic limitations and speech impairment and can allow for optimal oral hygiene. This results in more positive patient feedback and significant improvements in patient's compliance [10]. Additionally, the outstanding of CA compared to traditional orthodontic techniques is being able to view the result virtually before starting the treatment and the clinician can create multiple simulation plans with different treatment outcomes for patients to consider.

In two case reports, patients were positively and pleasantly satisfied with the convenience of using CA, while feeling more secure when receiving treatment with predicted results as well. They also mentioned that daily oral hygiene is a breeze; to clean their teeth, they only use a traditional toothbrush. At the same time, during the treatment process, when examining these two patients, we did not record any new tooth decay or current gingivitis. Indeed, with traditional fixed orthodontic appliances, oral health care is not easy. It requires more time and effort to maintain healthy oral health [11]. On the other hand, the smooth surface of the attachments adheres to the crown during treatment with CA reduces plaque accumulation and makes cleaning easier.

Otherwise, CA has disadvantages such as difficulty in root movement, tooth extrusion, high price, and not being recommended for all types of cases [12]. In our case reports, at the time of follow-up examination at tray no.27 (total 38 trays for upper) of patient no.01, off tray appears in both upper canines, that's mean they have not reached the position predicted by the ClinCheck©. At that time, the extrusion of teeth 13 and 23 was insufficient, and their roots are in unfavorable positions. The clinicians created a new plan to move the teeth, which was consistent with the current maxillary canine position but still did not affect the final simulation treatment results. For the patient no.02, off tray does not occur during the initial treatment period. But the root movement still does not move as planned. Therefore, a series of additional aligner is manufactured to improve the tooth root position. We can easily see that the unfavorable results of CA are inevitable. However, in reality, it is completely possible to overcome these disadvantages thanks to regular examinations to promptly detect unwanted errors. With the skills and knowledge of trained clinicians, it is possible to produce additional aligner to complete the treatment. To ensure effective results, it is necessary to understand the classification of the dentition condition in orthodontic and strictly follow the selection criteria of treatment indication in CA [7].

A study on orthodontic patients showed that both traditional treatment and CA treatment had the same complications of root resorption (with a light force about 25g) [13]. Therefore, although the CA feels gentle during treatment (because of its controlled force on each tray), it is necessary to inform patients about this disadvantage before choosing appliance treatment to avoid false expectations. Furthermore, the risk of relapse is still high after using CA, so retainers should be indicated after treatment.

IV. CONCLUSION

Through 2 cases above, it was noted that CA met the treatment needs of patients, brought comfort during usage and treatment duration is acceptable (less than 18 months). The final result achieve a healthy, functional and esthetic occlusion, combined with a harmonious facial appearance, which will remain relatively stable in the long run.

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Original research

OUTCOMES OF DUAL - MOBILITY CUP FOR DISPLACED FEMORAL NECK FRACTURES IN THE ELDERLY

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ABSTRACT

Background: *Femoral neck fracture (FNF) is a common intracapsular fracture in the elderly as a result of osteoporosis, which tends to increase with humans' extended longevity. Regarding treatment for undisplaced FNF, internal fixation is mostly used, while primary total hip arthroplasty (THA) is used for older patients with displaced FNF because of the high rate of avascular necrosis and nonunion. THA shows a better functional result than internal fixation in treating FNF; however, dislocation is still a severe complication. Recently, the dual mobility cup (DMC) has become more and more popular as a solution to reduce dislocation. The purpose of this research is to evaluate the outcome of dual-mobility cups for FNF in the elderly.*

Methods: *A retrospective study was carried out on 164 patients who had THA by means of a dual moblity cup and posterolateral approach in Hue Central Hospital from January 2018 to April 2023. Medical history, clinical and paraclinical features, and the modified Harris Hip Score (MHHS) were assessed. TraumaCad® software was used to measure the figures of hip prostheses.*

Results: *One hundred and sixty-four patients with a mean age of seventy-five years were followed up from 6 to 64 months. More than 90% of patients had osteopenia and osteoporosis according to bone mineral density. The average figures include length of incision (7,4 cm), operation duration (66,4 minutes), blood loss volume (664,6 ml), discrepancy of leg length under 10mm (97%); size of prothesis: shell (49,1mm), stem (11,6mm), head with short neck (90,2%). Radiological assessment showed that the mean abduction angle and anteversion angle were 48,1° ± 5,4° and 20.1° ± 5,6° respectively. There were four intraoperative calcar fractures (2,4%), three periprosthetic fractures (1,8%), no hip dislocation, no aseptic loosening and no infection. The overall MHHS was 92,1 ± 7.*

Conclusion: *DMC is an alternative option to prevent dislocation and give good outcomes to elderly patients with FNF. Longer follow-up duration may have revealed complications of DMC.*

Keyword: *Femoral neck fracture, dual mobility cup, total hip arthroplasty, American Society of Anesthesiology, modified Harris Hip Score.*

I. INTRODUCTION

FNF is an intracapsular fracture that commonly occurs in the elderly population due to osteoporosis. The average life expectancy of the population is increasing, leading to an upward trend in the incidence of hip fractures, estimated increase from 1.66 million people (1990) to 6.26 million people (2050) [1, 2].

Regarding the displaced FNF in the elderly, THA is increasingly being used in treatment compared to internal fixation having more risk of revision due to complications, such as pseudoarthrosis or avascular necrosis of the femoral head [3, 4]. Although hemiarthroplasty has a lower dislocation rate and shorter surgical time, it is usually used for patients with low active demand or accompanying severe comorbidities due to an early complication such as acetabular wear causing pain [5]. THA overcomes these limitations and provides better hip function

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compared to hemiarthroplasty, although it has a longer surgical time, higher blood loss, and higher rate of post-operative dislocation [6, 7]. According to a study by Iorio et al. (2001) [8] in elderly patients with FNF, the dislocation rates for total hip replacement and hemiarthroplasty were 10.7% and 2.9% respectively.

Therefore, DMC is considered as an alternative solution to standard hip prostheses in order to reduce the risk of dislocation in patients undergoing total hip replacement. According to a study by Adam et al. (2012) [9] on 214 patients with FNF, the dislocation rate of the DMC was 1.4% after a 9-month follow-up. In a study by Tarasevicius et al. (2010) [10] on the treatment of FNF using posterior approach, the dislocation rates for the dual mobility hip joint and conventional prosthesis were 0% and 14.3% respectively. This implant's stability comes from its unique design. The implant consists of two articulations, one which is not constrained between the acetabular cup and the mobile polyethylene liner, while the other is constrained between the femoral head and the mobile polyethylene liner.

The DMC was first used in France in 1977 and later widely adopted in Europe, but it was not until 2004 that it was approved for use by the U.S. Food and Drug Administration [11, 12]. Since 2015, the dual mobility hip joint has been utilized in total hip replacement surgeries at Hue Central Hospital in Vietnam. However, the surgical outcomes of dual mobility hip replacement in patients with hip fractures have not been fully evaluated. For these reasons, we conducted this research to evaluate the outcomes of total hip replacement using DMC in the treatment of elderly patients with FNF.

II. PATIENTS AND METHODS

2.1. Patients

This retrospective and non-comparative study was conducted on 164 patients (110 women, 54 men) who had THA of dual moblity cups in Hue Central Hospital from January 2018 to April 2023. Those chosen for this research were the elderly aged 60 and above having normal mobility before suffering the displaced FNF which is classified as Garden III - IV. The exclusion criteria include: pathological fractures of the femoral neck, acetabular reinforcement and hip arthroplasty after failure of internal fixation, associated fractures in the same leg with FNF, surgical risk by the American Society of Anesthesiology (ASA) from grade IV or higher, abnormal mobility before suffering the trauma.

2.2. Surgery

The same standardized surgical technique via a posterolateral approach was used for all patients. The cut level is calculated preoperatively by digital radiographs: $d = d_1 + d_2$ (Figure 1).

d: distance from center of rotation to lesser trochanter in normal femur.

d_1: femoral neck cut level (mostly 5mm)

d_2: length of femoral neck implant (only available in 45mm)

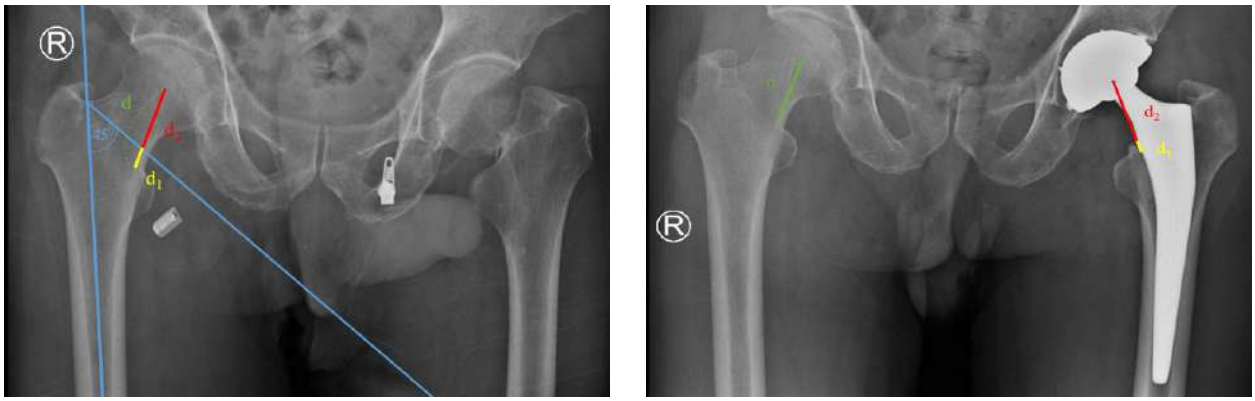

Figure 1: (a) preoperative X-Ray showing the position of femoral neck cut in normal femur and (b) postoperative X-ray with a DMC.

Soft tissues were repaired at the end of the operation. Second-generation cephalosporin antibiotic prophylaxis was performed 30 minutes before surgery and post-operative time. Enoxaparin by subcutaneous injection was used for prophylaxis of phlebitis during the hospitalization, while Rivarixaban was carried

out by oral for a period of 30 days postoperatively. All patients received the same rehabilitation program and weight-bearing immediately after surgery except in the event of intraoperative complications.

In this study, implants of Groupe Lépine including Quattro™ Vps Hap Cup PnP and Pavi™ Hap Stem 135° was used (Figure 2.). Cobalt chrome heads of 22 mm diameter were used for 44 mm and 46 mm diameter cups and 28 mm heads were used for 48 mm and more. The size of Polyethylene liner depended on the size of its cup and head.

Figure 2: Quattro™ Vps Hap Cup PnP and Pavi™ Hap Stem (Groupe Lépine)

2.3. Data collection and statistical analysis

The following intraoperative figures were collected: operation duration, length of incision, intraoperative complications, size of hip prosthesis.The postoperative parameters were gathered: estimation of blood loss volume (EBLV), 3 - day postoperative pain by Visual Analog Scale (VAS), discrepancy of leg length (DLL), postoperative complications and the position of DMC. TraumaCad® software is used to measure the anteversion and inclination angle of the cup, angle of femoral stem and DLL. Our research evaluated the hip function of patients based on a THA by MHHS. SPSS 26 software was used for the analysis.

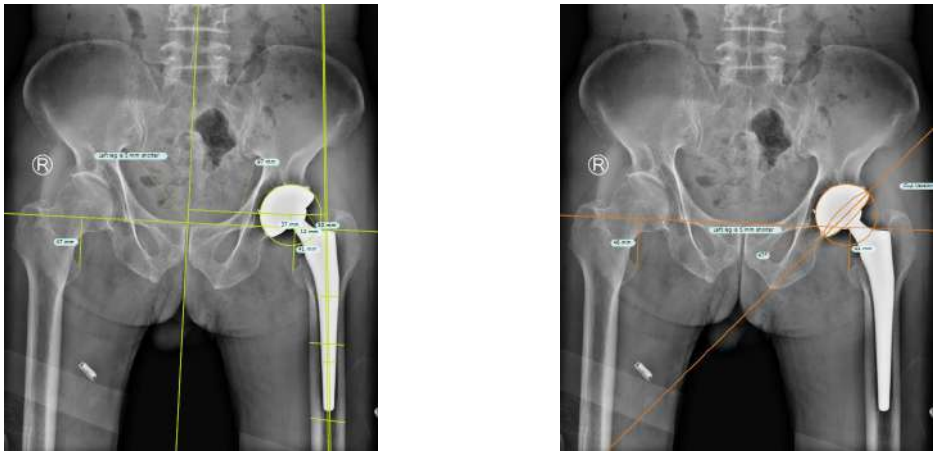

Figure 3: Evaluating the position of total hip prosthesis by TraumaCad® software

III. RESULTS

164 patients were included in the study with 6 - 64 follow-up months (Table 1). The mean age was 75.2 years ± 8.1 (60 - 91), with 67.1% of patients were females. At the last follow-up, 32 patients (19.5%) had died.

Table 1: General information about patients:

	# of patients n = 164
Age (years)	75.2 ± 8.1 (60 - 91)
Sex (male/female)	110/54
Side - Right - Left	 97 (59.1%) 67 (40.9%)
Mechanism of injury: falling	164 (100%)
Associated injuries: - Distal radial fracture - Proximal humeral fracture	 3 (1.8%) 1 (0.6%)
Death (%)	32 (19.5%)
BMI (kg/m^2)	21.6 ± 2.5 (16.5 - 27.1)
ASA - Grade I - Grade II - Grade III	 33 (20.1%) 70 (42.7%) 61 (37.2%)
Accompanying disease - Cardiovascular diseases - Endocrine diseases - Schizophrenia - Parkinson‘s syndrome - Other - No accompanying disease	 76 (46.3%) 42 (25.6%) 3 (1.8%) 5 (3.0%) 38 (23.2%) 33 (20.1%)
Bone mineral density at femoral neck (T-score) - Normal - Osteopenia - Osteoporosis	-2.4 ± 1.1 (-4.5 - 0.1) 14 (8.5%) 68 (41.5%) 82 (50.0%)

Approximately half of patients had cardiovascular diseases (46.3%), while schizophrenia and Parkinson‘s syndrome were found in 3 and 5 patients, respectively. 91.5% of our patients had an abnormal index for bone mineral density.

The average operation time was 66.4 minutes ± 12.5 (45 - 100), average length of incision was 7.4 cm ± 0.6 (6 - 9). Mean EBLV during the operation was 664.6 mL ± 456.5, needed blood-transfusion was n = 50 (30.5%). Mean hospitalization time was 11.7 days ± 2.5 (Table 2).

Table 2: General information

	n = 164
Operation time (minutes)	66.4 ± 12.5 (45 - 100)
Length of incision (cm)	7.4 cm ± 0.6 (6 - 9)
EBLV (ml)	664.6 ± 456.5 (29 - 1544)
Blood transfusion (%)	50 (30.5%)
3-day postoperative pain	2.4 ± 1.0 (1 - 5)
Postoperative time (days)	7.0 ± 1.5 (4 - 10)
Length of hospital stay (days)	11.7 ± 2.5 (8 - 17)

Regarding the size of prosthesis, mean sizes of cup and femoral stem were 49.1 mm ± 2.4 and 11.6 mm ± 1.1 respectively. Especially, 90.2% of patients used heads with short neck (-2 mm or -3.5 mm)

The radiological assessment was presented (Table 3).

Table 3: Radiology

	n = 164
Inclination (°) - Inside of range 30° - 50° - Outside of range 30° - 50°	48.1± 5.4 118 (72%) 46 (28%)
Anteversion - Inside of range 5° - 25° - Outside of range 5° - 25°	20.1 ± 5.6 139 (84.8%) 25 (15.2%)
Lewinnek's safe zone - Inside - Outside	 97 (59.1%) 67 (40.9%)
Angle of stem - Neutral - Valgus - Varus	 123 (75.0%) 34 (20.7%) 7 (4.3%)
LLD - < 5 mm - 5 - 10 mm - > 10 mm	 115 (70.2%) 44 (26.8%) 5 (3.0%)

There were four intraoperative fractures and three postoperative periprosthetic fractures (Table 4).

Table 4: Complications

Kind of complications	**n = 7 (4.2%)**	**Need for reoperation n = 2 (1.2%)**	**Way the complication was handled**
Calcar fracture	4 (2.4%)	0 (0.0%)	Cerclage
Periprosthetic fracture	3 (1.8%)	2 (1.2%)	Long cast, plate osteosynthesis, cerclage

During the surgery, four calcar fractures occurred while inserting the stem and were reinforced with cerclages around the trochanteric region. These patients had weight-bearing lately after 3 weeks. Three cases had periprosthetic fractures that occurred after several months (2 or 7 months) or 3 years after surgery due to a fall. Two of the three cases needed revision by plate osteosynthesis and cerclages keeping the stem in place and one case could be handled conservatively by cast. There were no dislocation, no thrombosis, no infection and no aseptic loosening in our study.

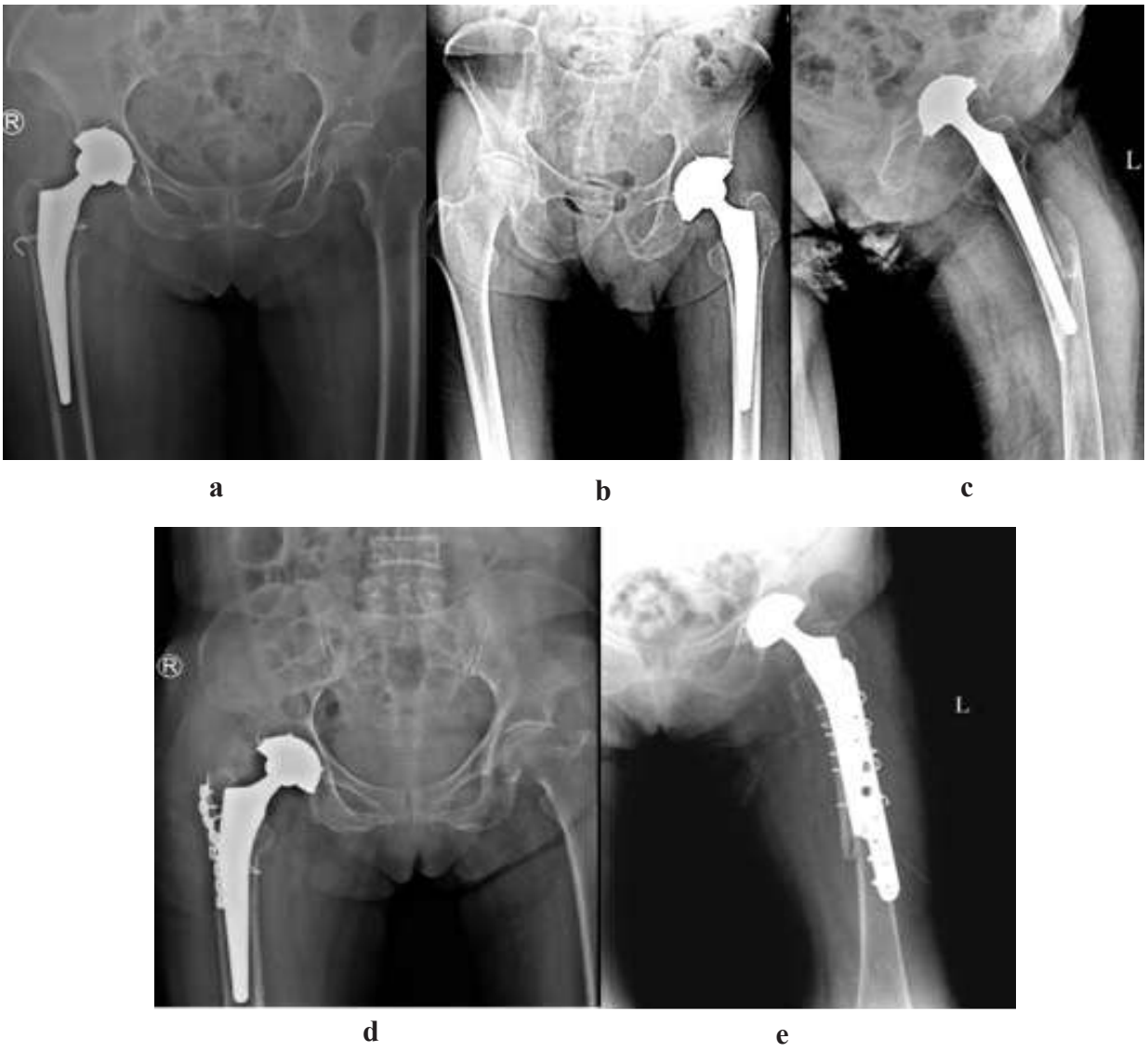

Figure 4: (a) Calcar fracture treated by a cerclage, (b) (c) periprosthetic fractures (d) (e) periprosthetic fractures treated by plate osteosynthesis and cerclages.

At the last follow-up, the mean MHHS was 92.1 ± 7.

Table 5. Comparison MHSS between age groups.

Age group	Modified Harris Hip Score			Total
	Fair	Good	Excellent	
60 - 69	2	8	38	48
70 - 79	4	15	31	50
≥ 80	8	15	11	34
Total	14	38	80	132
p = 0.0005				

The younger age group has significantly better hip function than the older (Table 5, with p = 0,0005).

4. DISCUSSION

There are several previous studies in the literature regarding the advantage of the DMC for THA, but there were just few studies describing the outcome exclusively for femoral neck fractures in the elderly treated by this procedure and this implant in Vietnam.

In our study, the main mechanism of injuries was falling, which 4 cases (2.4%) had upper limb fractures. In a study of almost 2,000 hip fracture patients, Robinson et al [13] reported an associated fracture or dislocation in just over 4% of cases. They are associated most commonly with upper limb fractures, mainly distal radial fractures and proximal humeral fractures. Patients with concomitant distal radial fractures were fitter than those with concomitant proximal humerus fractures and the latter group had a higher mortality rate [14]. In addition, more than 90% of our patients had a low bone loss mass (osteopenia and osteoporosis), which puts them at risk for fractures. Cummings et al. in a large study of bone density scans found that each standard deviation in femoral neck bone density increased fracture risk by 2.6 times after adjustment for age during an average follow-up of 1.8 years [15]. Therefore, after THA, doctors need to treat the osteopenia and osteoporosis for prophylaxis of second fractures.

In terms of accompanying diseases and ASA grade, most of the elderly had several comorbidities which was similar to another study [16 - 18]. Especially, 8 patients (4.8%) had Schizophrenia and Parkinson's syndrome. Currently, DMC is a well-accepted treatment option for any patient at an elevated risk for instability including patients with neuromuscular diseases, cognitive dysfunction, ASA score of 3 or more [11, 19].

There were outcomes of other studies using posterolateral approach (Table 5).

Table 6: Comparison

Authors	Age (years)	Patients	Operation time (minutes)	Length of incision (cm)	3-day post-operative pain	EBLV (ml)	Hospital stay (days)
Ait Mokhtar [20]	78	150	75	7	2.15	210	
Jaquot [21]	79	102	100	7		385	6.8
Macaulay [22]	82	17	89.1				7.7
Wani [23]	65	50	100				11.9
Our		164	66	7.4	2.4	363	11.7

Mean operation time was lower while figures for length of incision, EBLV and 3-day postoperative pain were quite similar to other studies (Table 6). Hospital stay is handled differently from country to country. Also, some of our patients had multiple accompanying diseases and required longer hospital stays for treatment.

A low dislocation rate was similar to authors using DMCs and lower than other studies using the same approach without DMCs (Table 7). In our study, most patients returned to usual daily activities with no limits of hip motion after 6 months. The same results could be observed in other studies [24, 25].

Table 7: Comparison

	Age (years)	Patients	Approach	Implant	Follow-up (months)	Dislocation (%)	HHS
Ait Mokhtar [20]	78	150	Postero - posterolateral	DMC	38	0.6	
Dorr [26]	69	39	Posterior	Not DMC	48	17.9	
Jaquot [21]	79	102	Postero - posterolateral	DMC	1.5	0	
Macaulay [22]	82	17	Posterola/ Anterolateral	Not DMC	24	5.8	84.2
Our		164	Posterolateral	DMC	6 - 64	0	92.1

The dislocation rate depends on many factors such as approach, surgeon experience, mini-invasive approach or not, etc. Following literatures and many studies, THA using posterior approach had a higher dislocation rate compared to anterior approach [14]. Despite our study used posterolateral approach and 40.9% of cup's positions were outside of Lewinnek safe zone, our dislocation rate remained 0% due to several reasons. The effectiveness of DMC was proved to reduce this proportion by many studies [9, 10]. Ait Mokhtar et al. [20] showed the dislocation rate was 0.6% in a 150 patients with 38 months follow-up. In addition, several findings reinforced the theory put forward by other authors that Lewinnek's safe zone is not specific enough to differentiate between stable and unstable THA implantations [27, 28]. Furthermore, a careful capsular repair and reattachment of the short external rotators were performed as part of our closure to minimize the risk of this complication.

Regarding size of prothesis, Vietnamese acetabulums were quite small with 82.9% under 52, while the large size of femoral stem could related to osteoporosis in the elderly. Surgeons mostly used heads with short neck due to the fact that angle 135° of femoral stem and neck made a longer DLL intraoperatively.

The immediate post-operative radiological analysis found no more than 4° femoral stem varus, which is quite similar to Grégoire Thürig et al. [29]. Most cases (97%) had the DLL lower than 1cm, compared to 100% in study of Ei Bitar et al. [30] and 85.9% in study of Ishii et al. [31].

Our intraoperative complications using the posterolateral approach were slightly lower than described in other study [29]. It was classified as A2 following Vancouver, meanwhile these patients had normal rehabilitation with the exception of not weight-bearing the first three-week postoperation.

The main cause for postoperative periprosthetic fractures is falling. Poor bone quality due to osteoporosis is as well a known risk factor [32]. Our incidence (1.8%) was lower than other studies with 4.1 % [33] or 6.9% [29]. Marsland [34] described that 70 % had, prior to a periprosthetic fracture, signs of stem loosening. For those who suffered femoral neck fracture, the risk of suffering a periprosthetic fracture is higher as well [32], [35, 36]. Recent evidence from large registries has shown that the key to prevent periprosthetic femur fractures is routine follow-up with radiographic studies [32].

Regarding several criteria of MHHS, the oldest group had lower scores due to the lack of self-confidence in walking without support or the fear of falling again while the younger ones could return to daily activities more easily.

V. CONCLUSION

In term of instability after primary THA, DMCs is more alternative in preventing dislocation and having good outcomes in elderly patients with FNF. Longer follow-up duration may have revealed complications of DMC. Reported outcomes of studies using DM cups with mid-to long-term follow up should be encouraged to support their effectiveness.

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REGULATIONS

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