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Optimal Grip Span for Measuring Maximum Handgrip Strength in Preschool Children

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Abstract

Background: Since the minimum grip span of a standard Smedley hand dynamometer is 4 cm, the handgrip strength (HGS) value at a less than 4 cm grip span has not been reported. **Objective**: The present study examined the impact of grip span on handgrip strength (HGS) in young children using a dynamometer ranging from 2 to 4.5 cm of grip span. **Methods**: A total of 93 (39 girls and 54 boys) children were recruited from a local kindergarten with the cooperation of their parents. Each participant performed one test trial and then five maximal trials using different grip spans (2.0, 3.0, 3.5, 4.0, and 4.5 cm) in random order and allowing a 1-minute rest between measures. **Results**: There was a statistically significant difference in HGS depending on which grip span was used, $\chi^2(4) = 211.5$ ($p < 0.001$). Mean ranks were 1.03, 2.79, 3.72, 3.94, and 3.53 for 2 cm, 3 cm, 3.5 cm, 4 cm, and 4.5 cm, respectively. Follow-up tests found statistically significant differences between each grip span comparison except for the 3.5 cm vs. 4.0 cm comparison ($p = 0.166$) and the 3.5 cm vs. 4.5 cm comparison ($p = 0.611$). Our finding showed that the highest HGS appeared at a grip span of 4.0 cm. In addition, the difference between HGS at a grip span of 4.0 cm and 3.5 cm or a grip span of 4.0 cm and 4.5 cm was statistically different but relatively small. **Conclusion**: Our results recommended that the target grip span for measuring maximal HGS in young children is about 4 cm (4 ± 0.5 cm).

Keywords

Childhood, Grip Span, Grip Strength, Hand Morphology, Reliability

1. Introduction

Muscle strength is a critical determinant of physical function. Skeletal muscle and the nervous system are two factors associated with muscle strength and both of these variables increase dramatically during development [1] [2] [3]. In studies of children, physical function (e.g., standing long jump and countermovement jump) is used as a surrogate when muscle strength cannot be measured directly [4]. When muscle strength is measured during development, it is typically assessed via handgrip strength (HGS) [5] [6] [7]. This is because HGS is a potential predictor of current and future health [8] [9] [10] and is associated with cardio metabolic and bone health outcomes in children [11] [12]. In addition, it is expected that measurements using a handgrip dynamometer will be actively used in research on early childhood in the future. Therefore, accurate measurement of a child's HGS is essential, but equipment for children is limited [13].

A standard model for measuring HGS is the Smedley hand dynamometer. The grip span is set before testing to adjust an individual's hand size with this device. However, the device was developed for adults. Thus, it has a limited range of grip span (≥4 cm) and may not be suitable for the hand size of young children. In addition, the device for adults has a HGS measurement range of 5 kg or more and cannot measure the HGS of some children. Using a Smedley hand dynamometer, several studies investigated the relationship between grip span (grip handle position) and HGS. When HGS is measured with grip spans of various lengths, the peak value of HGS appears at a specific grip span (*i.e.*, optimal grip span) compared with other measured grip spans. For example, Ruiz *et al.* [14] investigated the relationship between grip span and HGS of 30 men (mean age, 39 years old; range, 20 - 80 years) and 40 women (mean age, 41 years old; range, 20 - 80 years) and reported that there is an optimal grip span for both men and women. The same research group observed similar results for children (age range, 3 - 5 years) [15] and adolescents (age range, 13 - 18 years) [16]. The authors of those studies use hand size (*i.e.*, maximal hand width) to propose a standard grip span for measuring maximum HGS [14] [15] [16]. As mentioned above, however, the minimum grip span of a standard HGS dynamometer is 4 cm, so the optimal grip span remains unclear in studies of young children. In other words, in young children, the peak value may appear at the minimum grip span of 4 cm [15], and the HGS value at a less than 4 cm grip span has not been reported. We hypothesized that the peak HGS could appear with a grip span of 4 cm or less, given that young children's hand size is about half that of adults. Thus, the purpose of this study was to examine the impact of grip span on HGS in young children using a specially designed hand dynamometer (range of grip span, 2.0 - 4.5 cm).

2. Methods

2.1. Participants

A total of 93 (39 girls and 54 boys) Japanese children between the ages of 4.2 and

6.5 years were recruited from a local kindergarten with the cooperation of their parents (Table 1). Children with their parents were fully informed about the purpose of the study and its safety and written informed consent was obtained from the parents for each child. Participants did not include non-right-handers (left-handed or mixed-handed). This study received approval from the University's Institutional Review Board (HSS #29-17 & SG #2021-2-2).

2.2. Anthropometric Variables

Body mass and standing height were measured to the nearest 0.1 kg and 0.1 cm, respectively, by using a digital height and weight scale (DST-210S, Muratec KDS Corp, Kyoto, Japan). The forearm circumference of the right arm was measured at 30% proximal to the forearm length using a tape measure. We measured four different hand sizes using a ruler. Full hand length was measured as the linear distance between the distal wrist crease and the tip of the middle finger. Palm length was measured as the distance between the distal wrist crease and the midpoint of proximal flexion crease of the middle finger [17]. The index finger length was also measured as the distance between the tip of the index finger and the metacarpophalangeal joint flexion crease at the base of the thumb [18]. Maximum hand width was measured from the tip of the thumb to the tip of the little finger with the hand opened as wide as possible, and the distance between the two was measured to the nearest 0.1 cm [15].

2.3. Grip Span Measurements

Grip span was measured using a vernier caliper as the distance between the external bases of the grip to the central strip of the dynamometer.

2.4. Handgrip Strength Measurements

Maximum voluntary HGS was measured with the right hand using a Smedley handgrip dynamometer (TKK Grip-A, Niigata, Japan; ranges 0 - 30 kg strength and 2 - 5 cm grip span) [19]. All participants were instructed to maintain an upright standing position to keep their arms at their side. The participants held the dynamometer in the right hand with the elbow extended downward without squeezing. Each participant performed one test trial and then five maximal trials using different grip spans in random order and allowing a 1-minute rest between measures. The grip spans used were 2.0, 3.0, 3.5, 4.0, and 4.5 cm (Table 2). All the participants appeared motivated during the strength tests.

2.5. Reliability of Handgrip Strength Measurements

Test-retest reliability of HGS measurements using the intraclass correlation coefficient (ICC3,1), standard error of measurement, and the minimal difference (*i.e.* absolute reliability) was determined for data from an additional group of 13 young children (8 boys and 5 girls) tested twice, one week apart prior to the study. The same grip span for each participant was used at the test and retest measurements (setting grip span ranged 3.5 - 4.0 cm).

Table 1. Anthropometric variables of the participants.

	Girls	Boys	Overall
n	39	54	93
Age (years)	5.4 (0.8)	5.3 (0.8)	5.3 (0.8)
Height (m)	1.07 (0.07)	1.09 (0.07)	1.08 (0.07)
Body mass (kg)	18.0 (2.6)	18.8 (3.0)	18.4 (2.8)
Forearm length (cm)	14.4 (1.3)	15.0 (1.3)	14.7 (1.3)
Forearm girth (cm)	16.9 (1.0)	17.2 (1.1)	17.0 (1.1)
Hand length (cm)	12.0 (0.8)	12.4 (0.8)	12.2 (0.8)
Palm length (cm)	6.8 (0.5)	7.0 (0.5)	6.9 (0.5)
Hand width (cm)	13.9 (1.0)	14.1 (0.9)	14.0 (0.9)
Index finger length (cm)	7.3 (0.6)	7.5 (0.6)	7.4 (0.6)

Table 2. Handgrip strength with different grip spans.

	Grip span (cm)				
	2.0	3.0	3.5	4.0	4.5
Handgrip strength (kg)					
Girls (n = 39)	3.4 (1.3)	7.6 (2.1)	8.6 (2.4)	8.8 (2.7)	8.5 (2.9)
Boys (n = 54)	4.6 (1.4)	8.9 (2.1)	9.7 (2.2)	9.9 (2.6)	9.5 (2.7)
Overall (n = 93)	4.1 (1.5)	8.3 (2.2)	9.2 (2.3)	9.4 (2.7)	9.1 (2.8)

2.6. Statistical Analysis

Test-retest reliability was determined by calculating the difference between the values from the initial test to that of the retest. The standard deviation (SD) of that difference was divided by the square root of 2 in order to calculate the standard error of the measurement. The minimal difference (*i.e.* absolute reliability) was calculated by multiplying the SD of the difference by 1.96. Limits of agreement (95% level) were set by adding and subtracting the minimal difference value from the mean difference.

Differences in HGS were determined using the nonparametric Friedman test in order to obtain mean ranks. If there was a statistically significant result, pairwise comparisons were made using the Wilcoxin signed ranks test. Statistical significance was set at $p \leq 0.05$. The limits of agreement were calculated as noted before by taking the mean difference (e.g. 4 cm - 2 cm) in strength values. This allowed for a visual comparison between the strength differences in grip spans.

3. Results

3.1. Test-Retest Reliability

Paired t-tests revealed no significant differences between test [10.3 (SD 1.4) kg] and retest [10.1 (SD 1.1) kg], and mean difference was 0.18 (SD 0.82) kg. The correlation coefficient between the two tests was 0.815. The standard error of

measurement and minimal difference were, respectively, 0.58 kg and 1.60 kg. The 95% limits of agreement were 1.4, 1.7 kg.

3.2. Handgrip Strength with Different Grip Spans

There was a statistically significant difference in handgrip strength depending on which grip span was used, $\chi^2(4) = 211.5$, $p < 0.001$ (Figure 1). Mean ranks were 1.03, 2.79, 3.72, 3.94, and 3.53 for 2 cm, 3 cm, 3.5 cm, 4 cm, and 4.5 cm, respectively. Follow-up tests (Table 3) found statistically significant differences between each grip span comparison except for the 3.5 cm. vs. 4.0 cm comparison ($p = 0.166$) and the 3.5 cm vs. 4.5 cm comparison ($p = 0.611$).

The direct comparison between grip spans with the 95% limits of agreement is found in Figure 2. The dotted red-lines are the limits of agreement from the test-retest plotted to see how each difference compares with the error of the measurement itself. It is clear that using the smallest grip span produces lower estimates than the other four settings. All other comparisons produced varying level of estimates, with 4.5 cm and 4 cm being most similar.

Table 3. The results of the Wilcoxin Signed Rank Test. The median value for strength is represented in kg for each grip span ranging from 2 cm to 4.5 cm. Each grip span is compared with each other to determine how the ranks compare. – ranks denote how many participants had higher values on the second variable compared to the first variable (*i.e.* first variable vs. second variable), + ranks denote how many participants had higher values on the first variable compared to the second variable. Ties denote that how many participants did not differ. Z is the test statistic and an * means it was statistically significant at $p \leq 0.05$.

Grip Span	2 cm	3 cm	3.5 cm	4 cm	4.5 cm
Median (kg)	4.0	8.8	9.6	9.9	9.3
vs. 3 – ranks	92				
+ ranks	1				
Ties	0				
Z	−8.367*				
vs. 3.5 – ranks	93	68			
+ ranks	0	20			
Ties	0	5			
Z	−8.375*	−5.828*			
vs. 4 – ranks	93	68	50		
+ ranks	0	20	38		
Ties	0	5	5		
Z	−8.375*	−5.647*	−1.386		
vs. 4.5 – ranks	91	63	44	33	
+ ranks	1	29	48	54	
Ties	1	1	1	6	
Z	−8.322*	−3.874*	−0.508	−2.728*	

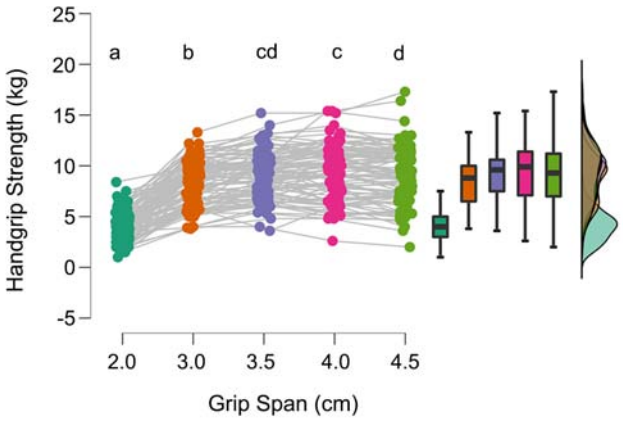
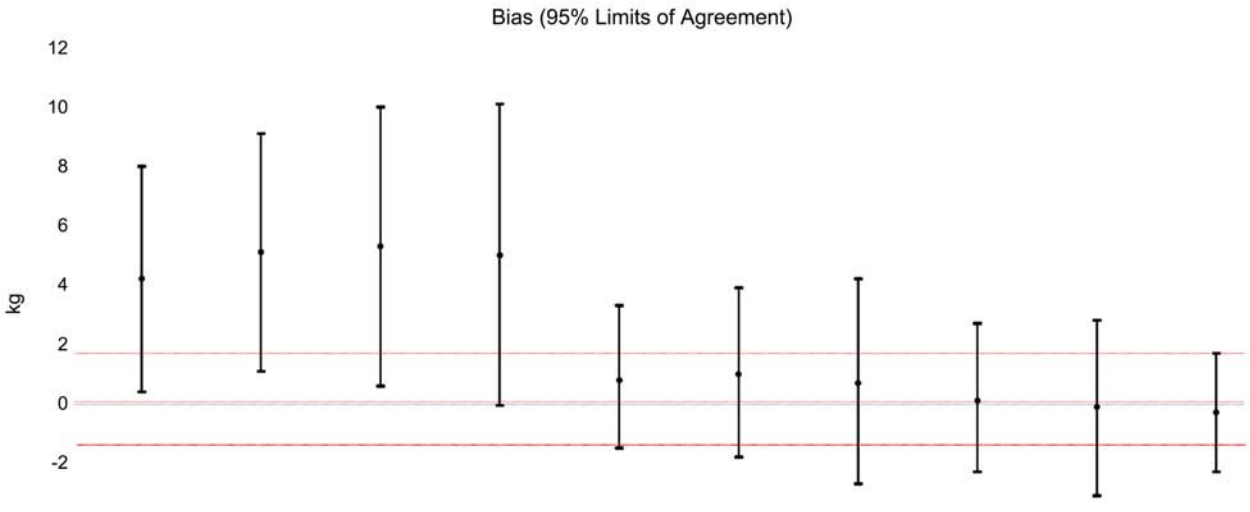


Figure 1. A comparison of handgrip strength (in kg) across the different grip spans ranging from 2 cm to 4.5 cm. The box pot represents the interquartile range of the difference and the cloud on the far right shows the distribution of the data. The letters above each grip span are there to denote which comparisons differ. Comparisons that share letters are not statistically different from each other (e.g. 3.5 vs. 4.5 share "d") and are not statistically different. Figure was made using JASP 0.16.3.



	3 cm vs. 2 cm	3.5 cm vs. 2 cm	4 cm vs. 2 cm	4.5 cm vs. 2 cm	3.5 cm vs. 3 cm	4 cm vs. 3 cm	4.5 cm vs. 3 cm	4 cm vs. 3.5 cm	4.5 cm vs. 3.5 cm	4.5 cm vs. 4 cm
Upper	8	9.1	10	10.0	3.3	3.9	4.2	2.7	2.8	1.7
Lower	0.4	1.1	0.6	-0.06	-1.5	-1.8	-2.7	-2.3	-3.1	-2.3
Mean	4.2	5.1	5.3	5	-0.8	1	0.7	0.1	-0.1	-0.29

Figure 2. The mean difference (in cm) between each grip span and the 95% limits of agreement of each comparison. The wider the bounds, the less agreement. The dotted red lines represent the limits of agreement to just taking the same measurement twice with the same device (*i.e.* there is some variability to just testing). The bottom includes the values used to create the figure. Upper represents the upper bound of the limits of agreement, Lower represents the lower bound of the limits of agreement, and mean represents the mean difference.

4. Discussion

The present study examined the impact of grip span on HGS in young children using a dynamometer ranging from 2 - 4.5 cm of grip span. The highest HGS

appeared at a grip span of 4.0 cm, and the difference between HGS at a grip span of 4.0 cm and 3.5 cm or a grip span of 4.0 cm and 4.5 cm was significantly different but relatively small, as described later.

As mentioned above, Sanchez-Delgado and colleagues [15] examined the association between grip span and HGS in children aged 3, 4, and 5. The authors used hand size (*i.e.*, maximal hand width) to propose a standard grip span for measuring maximum HGS. However, the grip span ranged from 4 cm to 6 cm, with a maximum HGS observed at 4 cm and a minimum HGS observed at 6 cm in all three age groups. Thus, the HGS value at smaller grip spans (<4 cm) was not investigated, although the hand size of participants was small compared with adults. In the present study, the highest HGS value appeared at 4 cm in the range of grip spans from 2 cm to 4.5 cm. The results from the present and previous studies suggest that the optimal grip span for young children (between ages of 4.6 and 6.5 years) would be approximately 4 cm.

Our findings showed that the difference in HGS between the grip span of 4.0 and 4.5 cm was 0.3 kg in boys and 0.4 kg in girls. Similar results were reported from a previous study [15] that the difference between the two grip spans (4.0 vs. 4.5 cm) was from 0.3 - 0.4 kg in boys between the ages of 3.5 - 5.6 years and 0.2 - 0.5 kg in girls of the same age range. In the present study, a similar phenomenon appeared in the difference in HGS between 3.5 and 4.0 cm grip span, and the difference was 0.2 kg in girls and 0.2 kg in boys (**Table 2**). Therefore, a difference of 1 kg or less was observed in HGS under conditions where the optimum grip span and the grip span of 0.5 cm are different. Importantly, the limits of agreement between 4 cm and 3.5 cm and 4 cm and 4.5 cm are relatively small compared to the test-retest reliability (**Figure 2**). When separated by sex, the limits of agreement were visually similar (data not shown). In addition, previous studies have confirmed similar results in adults [18] [20]. Those studies reported that the peak value of HGS was observed at the optimal grip span and that there were similar HGS values at 0.5 cm narrow or greater in width from the optimal grip span.

On the other hand, several studies have investigated the optimal grip span for measuring maximum HGS in children aged 6 to 13 years [21], adolescents [16], and adolescents with down syndrome [22]. Those studies compared the HGS at the optimal grip span with the HGS at 1 cm shorter or longer than the optimal grip span. When it was 1 cm shorter than the optimal grip span, the HGS was significantly lower, and the difference between the two was about 2 - 3 kg [16] [21] [22]. Considering that children and adults have different optimal grip spans [16] [21], hand size influences the difference. We found mean differences between our optimal grip span of 4 cm and the smaller grip spans. The difference between 4 cm and 2 cm grip spans was pronounced and was post-hoc found to be related to the size of the hand ($r = 0.425$, $p = 0.003$). In other words, as the size of the hand increased, the greater the difference was between the 4 cm and 2 cm grip spans.

5. Conclusion

The current study examined the impact of grip span on HGS in young children using a dynamometer ranging from 2 - 4.5 cm of grip span. The highest HGS appeared at a grip span of 4.0 cm. In addition, the difference between HGS at grip span 4.0 cm and 3.5 cm or grip span 4.0 cm and 4.5 cm was significant but relatively small. Our results recommended that the target grip span for measuring maximal HGS in young children is about 4 cm (4 ± 0.5 cm).

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Multiple Myeloma in a Patient with Rectal Cancer

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Abstract

Multiple myeloma is characterized by the accumulation of clonal, malignant plasma cells in the bone marrow. Multiple lytic skeletal lesions in some tumor patients with multiple myeloma are easily considered as bone metastases secondary to tumors, resulting in a missed diagnosis of multiple myeloma. Herein, we report a rare case, in which rectal cancer with multiple myeloma was initially misdiagnosed with bone metastases secondary to rectal cancer, due to the symptoms of multiple lytic sketetal lesions, and ignoring the abnormal plasma cells in the peripheral circulating blood smear. The patient was finally diagnosed with coexistence of rectal cancer and multiple myeloma. The case focuses on the importance of the peripheral circulating blood smear detection.

Keywords

Multiple Myeloma, Multiple Lytic Skeletal Lesions, Plasma Cell

1. Introduction

Multiple myeloma (MM) is the second most common hematologic malignancy [1]. It is mostly observed in older adults with a median age of 66 to 70 years [2]. MM is characterized by the accumulation of clonal, malignant plasma cells in the bone marrow [3]. It can affect many areas of the body, such as the bones, kidneys, eyes, and nerves [4]. In the majority of patients, malignant proliferation of plasma cells causes the M protein (abnormal IgG, IgM, or IgA or rarely IgE or IgD) in the serum and/or urine [5]. Multiple myeloma cells also produce abnormal light chain proteins (κ or λ). Therefore, the multiple myeloma process causes an excessive M protein level which leads to hyperviscosity [6]. Many symptoms of MM are vague. Patients may feel tired, unexplained weight loss, get frequent infections. Some patients even have no symptoms [7]. The uncontrolled

growth of malignant plasma cells results in hypercalcemia, renal failure, anaemia, or destructive bone lesions ("CRAB") [8] [9]. Pathological fractures may occur in the skull, spine, pelvis rib cage and the long bones. Many patients will often present with new bone pains or pathological fractures [10]. However, for some patients with tumors, bone is the most frequent site for metastasis [11]. These patients may present bone destruction. Therefore, multiple lytic skeletal lesions in some tumor patients with multiple myeloma are easily considered as bone metastases secondary to tumors, resulting in a missed diagnosis of MM. Herein, we report a case, in which rectal cancer with MM was initially misdiagnosed with bone metastases secondary to rectal cancer, due to the symptoms of multiple lytic sketetal lesions, and ignoring the importance of the peripheral circulating blood smear detection.

2. Case Description

A 78-year-old man was diagnosed with rectal cancer at the local Hospital in 2017 and underwent radical surgery for rectal cancer, followed by postoperative chemotherapy for 6 rounds. He was referred to the respiratory department of our hospital due to fever and cough on July 15, 2021. CT showed multiple lytic skeletal lesions involving the spine, ribs and skull and vertebral compression fractures. Multiple postoperative bone metastases from the rectal cancer were diagnosed mainly involving the spine, ribs and skull. Routine blood specimens from this patient were tested in our laboratory. CBC showed a leukocyte count of 13.2 $\times 10^9$/L (reference value: 3.5 $\times 10^9$/L - 9.5 $\times 10^9$/L), a hemoglobin concentration of 63 g/L (reference value: 130 g/L - 175 g/L) and a platelet count of 60 $\times 10^9$/L (reference value: 125 $\times 10^9$/L - 350 $\times 10^9$/L). The peripheral blood smear showed plasma cells that contained round inclusions (Russell body), known as Motto cells (**Figure 1**). These changes are related to abnormal synthesis, trafficking or excretion of the immunoglobulin that is stored in excess within the cytoplasm [12]. Therefore, we suspected that the multiple lytic skeletal lesions were not bone metastases but were actually caused by multiple myeloma. Therefore, we continued to follow up on the other test results of this patient. Biochemistry showed total protein 131.60 g/L (reference value: 60 g/L - 80 g/L). Serum and urine electrophoresis demonstrated a monoclonal protein. Serum immunoglobulin showed IgG 135.00 g/L (reference value: 7.51 g/L - 15.6 g/L), IgA < 0.0667 g/L (reference value: 0.82 g/L - 4.53 g/L), IgM < 0.0417 g/L (reference value: 0.46 g/L - 3.04 g/L), β_2-microglobulin 9.35 mg/L (reference value: 0 - 2.8 mg/L), serum free λ light chain 164.00 g/L (reference value: 3.13 g/L - 7.23 g/L), serum free κ light chain 0.22 g/L (reference value: 6.29 g/L - 13.5 g/L), urine free λ light chain 115.00 mg/L (reference value: 0 - 3.9 mg/L), and urine free κ light chain < 6.940 mg/L (reference value: 0 - 7.1 mg/L). Multiple myeloma IgG-λ type was subsequently diagnosed.

3. Discussion

MM is a type of haematological bone marrow malignancy. According to typical

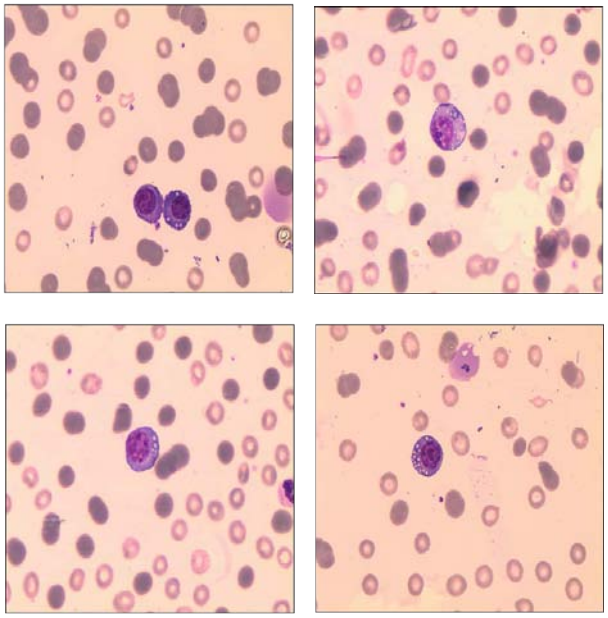

Figure 1. Motto cells containing round inclusions (Russell body) in different field of peripheral blood smear (×1000, Wright Giemsa).

symptoms and investigations, MM can be easily diagnosed for hematology specialists. However, for the non-specialist, MM or even coexistence of solid tumor and multiple myeloma is easily misdiagnosed or missed. Many patients with multiple myeloma initially present with bone pain involving long bones, rib skull, and pelvis. For many cancer patients, once cancer spreads to the bone, it is rarely cured and is associated with the symptoms including pain, increased risk of fracture, and hypercalcemia [13]. These symptoms are similar to the symptoms of MM. Therefore, multiple lytic skeletal lesions in some tumor patients with multiple myeloma are easily misdiagnosed with bone metastases secondary to tumors, resulting in a missed diagnosis of multiple myeloma. Herein, we report the case, in which rectal cancer with multiple myeloma was initially misdiagnosed with bone metastases secondary to rectal cancer, due to the symptoms of multiple lytic sketetal lesions, and ignoring the importance of the peripheral circulating blood smear detection. The abnormal plasma cells in the peripheral blood smear is a persuasive sign for a suspected diagnosis of MM. The presence of a high paraprotein and/or skewed imbalance of the κ/λ ratio is highly suggestive of diagnosis of MM.

4. Conclusion

In clinical practice, some tumor patients with multiple myeloma are easily misdiagnosed with bone metastases secondary to tumors, resulting in a missed diagnosis of multiple myeloma. However, the coexistence of more than two kinds of tumors is not common, which can easily lead to clinical neglect. Therefore, we should pay attention to the hematological examination while performing the imaging examinations. The examination of peripheral blood smears is not only

essential for diagnostics of hematological diseases but can also provide vital indications for the other diseases. By the systematic analysis of peripheral blood smears for alterations to blood cells, a blood smear test can make an important contribution to the formulation of a diagnosis [14]. Therefore, peripheral blood smears are an important screening method and should always be considered [15].

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Berrettini Anastomosis Iatrogenic Injury Relating to Carpel Tunnel Syndrome Case Study

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Abstract

Some diseases require medical mitigation following the diagnosis, and sometimes the situation means that the patient has to undertake strong medication. However, this medicine is designed pharmacodynamically to interact with other organs before they reach the intended organ. Some mitigation imposes challenges on the involved organ. While the main organ will be healed, some drugs' footprints will be left out to other organs. These are called iatrogenic injuries. In the case of anastomosis, it requires the alteration of surgical methods or the origin of iatrogenic injury in the arm; thus, the knowledge of anastomosis is very important to the field of medical practice. In addition, carpal tunnel release becomes vital in curing carpal tunnel syndrome. The paper focuses on a case of a 42-year-old woman found to have a complication to her middle finger. This case becomes important for studying Berrettini anastomosis iatrogenic injury, which relates to carpal tunnel syndrome. The Berrettini branch is a complication that facilitates communication between the superficial ulnar and median nerve. The analysis also provides the electro-diagnostic evidence of Berrettini anastomosis on how it can give a position three-finger and thus contribute to a force explanation of the median neuropraxia. Lastly, the paper provides information on the implication of the Berrettini branch for surgical use. The implication of pictures in the digital era can be used to analyze the varied connection and length between the median nerve and ulnar section. It's easy to locate the position of high risk of iatrogenic injury in the palm due to the consistent location of Berrettini communication branches. The precaution is that operations have to be conducted moderately for a clear vision as the carefully mitigated practice ensures protection from the destruction and injury of the surrounding structures.

Keywords

Iatrogenic Injury, Berrettini Anastomosis (BA), SNAP-Sensory Nerve Action

Potential, CTS-Carpal Tunnel Syndrome, Median Nerve, Ulnar Nerve

1. Introduction

Iatrogenic injury is organ or tissue damage that results from pharmacotherapy, necessary medical treatment, or may be from using medical devices that have no relation to the primary disease. This injury that emerges from applying some drugs fairy interacts with the other organs, for instance, the skin, subcutaneous layer of tissue or even tissues found amerced down the skin layer. When these organs are compromised, they result in something different called iatrogenic wounds. This injury can be intense depending on the disease or the depth of the medicine used to cure the organs. The point to note is that the iatrogenic injury results from the necessary treatment of a particular condition but the medicine also affects other organs. Berrettini's anastomosis has been identified as the most encountered condition and is described as a neural connection between the common digital nerves in the median nerves and the ulnar.

The altered innervation sequences of the musculoskeletal complication of the forearm and hand have misleading symptoms. In addition, when anastomosis appears, it requires altering surgical methods or being the origin of iatrogenic injury; therefore, this information about anastomosis is important to medical practice. Carpal tunnel release is used to treat and heal a painful complication called carpal tunnel syndrome [1]. In carpal tunnel release, a cut is made via the ligament presses down the carpal. The condition makes more room for the tendon and the median nerve that cuts across the tunnel and upgrades suffering and functionality. The paper is a case study set up, and the main objective is to discuss digging more information on the iatrogenic injury of Berrettini anastomosis during carpaltunnel syndrome.

2. The Case of Study of the Patient

The case in the study involves a woman, 42 years old. The woman has no history of high blood pressure or diabetes. She was a housewife and gave care to two kids. The subject developed a complication of numbness and tingling, sensation in the thumb and digits; thus, it was hard for her to carry out her daily chores. Afiel surgical operation released the complication of numbness in her middle finger. After a pre-operation examination, the range of motion was complete, and the tinned sign returned positive. Also, the Afiel post-operation, as well as numbness, was present, but signs test of Phalen came out absent. Thus this case will be used to document Berrittini anastomosis iatrogenic injury in the case of releasing of carpal tunnel.

Since it's documented on the existence of the nerve communication between ulnar to the median nerve and how it results to correct and counterintuitive conclusion to carry out release of carpal tunnel, its possibly true that failure to

produce a correct physical examination may result in diagnosing a patient with carpal tunnel syndrome which is not the case [1], in the long run, this contrasting-information indicate that the patient will not be diagnosed with the right complication and thus not treated accordingly. The berrettini branch, which is often referred to as superficial ulnar to median nerve communication in hand, is a form of pure sensory communication and occurs in most cases. Its injury during the carpel tunnel release can alter the middle ring and figure sensibility. The use of electro-diagnostic clues has identified the median nerve communication, but for neurophysiologists, they are inconclusive since they may fail to identify the unusual observations. In addition, the process is involved errors from the systems being used to give information, but sometimes they may give irrelevant communication. The observer/researcher can have the information presented, giving conclusive and self-satisfactory evidence for a sensory ulnar-to median nerve communication distal that is directed to the elbow. Such details can be useful when performing surgical decision-making despite most neural variations being anatomical, phylogenic and having neurophysiologic interest instead of medical knowledge.

2.1. Electro-Diagnostic Evidence of Berrettini Anastomosis

Median sensory nerve conduction studies in carpal tunnel syndrome can be undertaken on any figure, but this depends on the patient's and physical preference. Researchers and medical practitioners often employ digital techniques, for instance, digital median sensory nerve action potential evaluation that is associated with some challenges depending on the choice of the digit of preferences [2]. For instance, the measurement error minimizes the measurement error by using the third digit figure being the longest and the largest and thus associated with its size. The finger also has the highest number of presentable nerve courses, therefore vulnerable to carpal pressure due to its strategic position in the palm. Finally, there may be a challenge in the overstimulation of the wrist median nerve that results in fibers depolarization that cross to the third figure. Some patients with severe median neuropathy, while their test for the median sensory nerve action potential is negative, maybe result additional challenges. Thus, it can be concluded that stimulation of the Berrettini anastomosis (BA) gives a digit three-finger and thus contribute to a force explanation of median neuropraxia.

The aspect of palm and hand in various cases reported in anatomical data readable by health practitioners is described as the potential for description for Berrettini anastomosis. This complication is mostly observed in 60% of the general cases; thus, the health caregivers consider it a normal occurrence and anomalous. The Berrettini is more often considered sensory and gives a certain percentage of sensory axons found in the ulnr through the wrist to the palm. To evaluate the ulnar diversion to the medial part, the third normal palm nerve Ferrari and Gilbert did a minute anatomical analysis of Berrettini anastomosis.

In their studies, they used dead bodies to observe fiber distribution. However, their sample size was not large enough, and they failed to introduce a foundation of ulnar section in Berrettini anastomosis [2]. The presentation of the sensory nerve action represented as D3 (third digit), as well as a different case presented in the lateral D3, had their representation as the third decile and the overall total digital nerve fiber. The details of ulnar SNAP transection in the palmar part originating from the palm indicate that the palm stimulation strategy in carpal tunnel can be used to hinder the block responsible for the conductive activity and thus gives a negative outcome. There are even more severe cases of carpal tunnel where the median wrist stimulation gives no results. Therefore there is a possibility of extreme stimulation at the hand joint position and ulnar nerve depolarization resulting from the conduction and CTS improper result description.

The evidence of electrodiagnostic evidence of Berrettini anastomosis relates to the dissections that reveal ulnar sensory crossover, which is referred to as the normal anatomy. However, the quantity of research on electro physiologic information is scarcely documented [2]. In the study of various patients, the third position of their Berrettini is measurable in repeated electro-diagnostic nerve conductivity. The observed latency is constant, while the magnitude is less compared to the ulnar sensory response. Also, the information on the clinical importance of the Berrettini in relation to sensory is non-clear. The existence of Berrettini anastomosis in extreme carpal tunnel syndrome can produce less normal latency sensory retreat that can be interpreted and result to undesirable information.

2.2. The Implication of Carpel Tunnel Release on the Branch of the Berrettini Anastomosis

The important part is that carpal tunnel syndrome is curable, and the simpler way is through surgical operation applying for open and endoscopic release. These two techniques are long-term but have no same because the endoscopic carpal release is related to a lower tendency of additional complications and a faster resume to function for the patient's hand [3]. These strategies have been linked to high iatrogenic injury of the Berrettini anastomosis branch, also termed as communications of palmar region between the medial and ulnar nerve, which affect the middle and the ring finger. This will be possible to know how often the Berrettini occurs and how it may result in iatrogenic injury. The author describes the requirement to successfully evaluate the magnitude of Berrettini anastomosis occurrence in various segments. Proper grouping of the specimen (hands) requires that hands be grouped into four categories per of Ferrari and gilbert scheme. In the observation that was carried out, the author records that group 1 consisted of hands in which communication was directly oblique between the median nerve to the ulnar at an angle of less than 55 and the distance between the distal and the origin of communication on the TCL end to be greater than 4 mm. In the second group, the specimen (hands) involved have a direct communication parallel to the far margin of the TCL and are kept lower

than 4 mm at a right angle to the ulnar nerve. The third group had hands whose communication ranges from the third common digital nerve to the ulnar, having an acute angle and the origin from the distal margin to the ulnar on the TCL end is below. The final group of the specimen consisted of hands that linkage is directed from the ulnar to the median nerve and have more than one branch of communication, but in this particular case, it was hard to obtain such hands; there is also total confidence of the report that was obtained due to the involvement of an independent observer.

According to the author, the Berrettini branch can be seen as normal observation, not a variation or anomaly. This study presented a fair finding compared to Shan and meals. The name Berrettini branch came to existence in the field of medicine in 1991, introduced by meals and Calkins. Also, the identification of communication between the ulnar as well as the median nerve was introduced by Pietro da cortina [3]. In classifying the four types of communication, all credit is given to Gilbert and Ferrari because, contrary to the previous researchers, they classified communication into four distinct groups while the others had classified communication into two distinct groups. The analysis in the discussion identified that the third group was seen to be most frequent, having a percentage of 65% compared to those of Ferrari and Gilbert, representing 30%. Communication or relaying information from the ulnar and median nerve is associated with some features. The ulna region of the middle finger and the ring finger of the radial part make up the sensory branch of communication, and this section becomes their main innervation distribution. In addition, when the patients are suffering from Berrettini anastomosis, they are said to have an uncomfortable tingling sensation in the radial half of their ring finger and the corresponding ulnar median finger. This sensation was thus described before ECTR came to action. The valls-sole employs electrophysiological findings to explain the hidden concept of communication between the median and ulnar nerve that operate in hands; he claims that the linking of information uses fibers running within the ulnar nerve to the distal wrist crease, and thus this knowledge would help to determine if the patient has Berrettini branch even before performing the surgical process.

2.3. Berrettini Branch Implication for Surgical Use

In the study under observation, there was a classification of analysis up to four groups. From the study, the learner can articulate that the Berrettini branches were identifiable in groups one and two in 28%. They were observed to be located on the distal incision, and therefore the patients are seen to be exposed to iatrogenic injuries [3]. Additionally, the branches can be observed when scalpel is removed during single portal ECTR. The normal BB (Berrettini branch) has been found away from the surgical area and is not subject to injury. The researcher could recommend that the hands and Berrettini branches, which were identified as group two, are the safest strategies to use when performing this sur-

gical operation since the activity does not necessarily result in iatrogenic injuries and because also they have ligaments incisions that come from central section and have a section that extends to nearer and as well as away sections of the hand palm.

Another implication is that the digital pictures showing dissected palms can be analyzed to define the length and position of superficial connections involving both the ulnar and the median nerve [4]. When a specific coordinate having seven specified landmarks is used to define its position, the Berrettini communicating branches are observed to be located consistently. Therefore it becomes easy to identify a high-risk area in the palm. This helps in knowing the region of a high-risk zone and can be applied to evade the risk of iatrogenic nerve injury. The precaution is that an operation on the palm must be conducted moderately to have a clear vision. This practice also protects against the possible destruction of the surrounding and unusual structures.

2.4. Interventions and Possible Treatment

There are other cases where there is an application on steroid injections being used frequently to treat carpal tunnel syndrome [5]. This intervention has been described as safest with reduced risks. The nature of iatrogenic median nerve injury is rare but rarely known with well-identified complications. It happens due to neural injection between the corticosteroids and results in nerve pain and damage. The patient hardly experiences tingling, numbness or pain at the time of injection until 24 hours after injection. The use of steroid injection can influence suspecting carpal tunnel but in the acute form. This makes it important for the health practitioners to involve the patients in the discussion on the possible occurrence of acute CTS and thus mitigate the event of permanent nerve damage.

2.5. Patient's Perspective after Treatment

Some patients believed that Berrettini affects them and is associated with painful neuroma formation or may be happening due to sensibility in the central figure's middle ulnar side or radial side. The patients can comfortably feel pain relieved between 3 to 5 hours and thus able to operate a computer mouse and perfume their daily activities like eating and driving. The patients can also comfortably use the machine for several days but with some restrictions.

3. Conclusion

It's good for health practitioners and patients to articulate the need to conduct a thorough medical analysis of the peripheral nerves. This should be done by relating and applying knowledge to electrodiagnostic studies. Also, the occurrence of unusual feelings and conditions should be used as hints, and an electrophysiologist should properly address the variations between the physical and historical data.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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Platelet-Derived Growth Factor-A Overexpression Correlates with Atrial Fibrosis in the Patients with Atrial Fibrillation Secondary to Rheumatic Valvular Disease

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Abstract

Objective: To investigate the relationship between platelet-derived growth factor-A (PDGF-A) and atrial fibrosis in patients who have developed atrial fibrillation (AF) secondary to rheumatic valvular disease. **Methods**: 84 selected patients participated in the current study who have developed rheumatic heart disease and were going to have a cardiac surgical operation. In the current study, whole subjects were divided into two group, they were atrial fibrillation (AF) group (the quantity is thirty-nine) and sinus rhythm (SR) group (the quantity is forty-five). Before the operation, complete clinical data was available for the whole patients. During the operation, the right atrial tissue (0.3 - 0.5 mm^3) was disserted from every patient. Right atrial fibrosis was observed by Masson staining and the distribution of PDGF-A in right atrium specimen was observed by immunohistochemistry. RT-PCR techniques were applied to admeasure the mRNA expressions of PDGF-A in patients' atrial tissue. At the same time, western-Blot techniques were employed to admeasure the protein expressions of PDGF-A. **Results**: In baseline clinical characteristics, in both AF group and SR group, there was no apparently difference between them ($P > 0.05$); compared with SR group, the diameters of left atrium and right atrium in AF group were apparently increased ($P < 0.05$). The results of Masson staining revealed that the atrial tissue fibrosis was clearer in AF group, and collagen volume fraction in the AF group was evidently exceeding SR group ($P < 0.05$). The expressions of PDGF-A's mRNA and protein from right atrial tissue in the AF group were evidently greater than SR group ($P < 0.05$). The mRNA and protein expressions of PDGF-A and the right atrium diameter go hand in hand. **Conclusion**: Atrial

remodeling plays an important role in patients with valvular atrial fibrillation; PDGF-A in patients with AF was highly expressed in the right atrial, and was closely related with atrial fibrosis.

Keywords

Atrial Fibrillation, Platelet-Derived Growth Factor-A, Collagen Volume Fraction, Atrial Fibrosis

1. Introduction

The most common supraventricular arrhythmia in the world is Atrial fibrillation (AF), which is characterized by rapid and irregular activation of the atrium [1] [2].

Several cardiovascular disorders predispose to AF, such as valvular heart disease [3], coronary artery disease, congestive heart failure [4] [5], and hypertension. The most important histopathological change in atrial fibrillation is atrial fibrosis which involves a disproportionate excessive accumulation of extracellular matrix [6] between muscle fibers and around blood vessels. Atrial fibrosis underlies atrial structural remodeling [6] [7] and reportedly contributes to the development and maintenance of AF [8] [9]. Although, it is not clear for the precise pathophysiological mechanisms, it has been proposed that extracellular matrix-modulating enzymes, cytokines, growth factors, and components of the fibrinolytic system play considerable roles in AF.

Platelet-derived growth factor-A (PDGF-A), a member of the PDGF/vascular endothelial growth factor family [10], is highly expressed in the myocardium throughout development and adulthood [11]. PDGF-A solely binds to PDGF receptor-α (PDGFR-α), and subsequently activates several intracellular signaling cascades, then stimulates growth, differentiation and migration of cells [10] [12]. It is known that PDGF-A and PDGFR-α are essential for the development of support cells in the vasculature, and involved into tissue fibrosis. However, it is not well investigated whether they contribute to atrial fibrosis. In order to determine whether PDGF-A participates in atrial fibrosis associated with AF, we investigated the expression and distribution of PDGF-A in patients with and without AF.

2. Materials and Methods

2.1. Patient Enrollment and Data Collecting

84 consecutive patients with rheumatic heart disease (RHD) who were going to undertake cardiac surgery were enrolled in this study at First Affiliated Hospital of Xi'an Jiaotong University, Xijing Hospital and Shanxi Provincial People's Hospital in 2012. All patients consecutively underwent simple mitral valve replacement surgery.

Baseline demographics, physical examination, routine laboratory testing, echocardiography, and additional clinical data were available for all patients before surgery.

84 selected patients were divided into two group, they were atrial fibrillation (AF) group (the sample size is thirty-nine) and sinus rhythm (SR) group (the sample size is forty-five). The subjects were considered eligible to be enrolled into the AF group if they had obvious AF history and had been documented by electrocardiogram with AF for more than 6 months. The SR group is composed of patients who is sinus rhythm and without history of atrial fibrillation.

Before surgery, no patients received any type of angiotensin receptor blockers (ARB) or angiotensin-converting enzyme inhibitors (ACEI) for at least six months, and none of the subjects had taken anti-inflammatory drugs previously more than two weeks before the study. In the present study, we excluded the patients as follows: 1) patients who exceeded 65 years old or had a history of cancer; 2) patients with complicated diabetes, renal or liver failure; 3) patients with hyperthyroidism, hypertension, autoimmune disease; 4) patients with heart failure over New York Heart Association (NYHA) III or left ventricular ejection fraction (LVEF) less than 40%, and other heart diseases; 5) patients who suffered rheumatic fever in active stage.

Before they take part in this investigation, every selected patient has signed informed consent forms that obtained from every selected patient or their family members. All informed consent forms and the procedure protocols were authorized by the Ethics Committee of the First Affiliated Hospital of Xi'an Jiaotong University. The investigation tallies with the principles outlined in the Declaration of Helsinki.

2.2. Human Cardiac Tissue Collection and Storage

All patients underwent cardiac surgical operation with moderate hypothermia (33˚C - 34˚C) and the right atrium (RAA) tissue (0.3 - 0.5 mm^3) was disserted during the surgery. Each piece of tissue was cut immediately into three parts. One was dropped into liquid nitrogen and then stored in the −80˚C for RT-PCR and Western blot. Samples for immunofluorescence were promptly implanted into Tissue OCT-Freeze compound, flash frozen, and cut into 10-μm sections using Cryostat at optimal cutting temperature. All tissue sections were stored at −80˚C until they were used for immunostaining and analysis. The third was fixed in 4% paraformaldehyde solution for 12 - 24 hours, imbedded in paraffin with Masson's trichrome staining.

2.3. Masson's Trichrome Staining and Collagen Volume Fraction Assay

The specimens fixed in 4% paraformaldehyde were subjected to alcoholic dehydration and embedded in paraffin. 4 μm serial sections were sliced and subjected to Masson's trichrome staining to highlight collagen fibers. Collagen volume fraction (CVF) assay was performed in tissue sections of the right atrium. Mas-

son's trichrome a was obtained from Boster Biological Engineering Corporation (Wuhan, China). Two slides of each sample were randomly selected and observed under polarization microscope. Six different vessel-free fields (×200) of each slide were captured, and the images were analyzed using Image Pro Plus 6.0 (IPP 6.0) software. Collagen volume fraction was showed as the percentage of area of positive collagen staining in the total area of the image. The following formula was used to calculate the fibrosis score: collagen fiber area/total view area × 100%.

2.4. Detection of Positive for PDGF-A by Immunofluorescence Staining

The right atrial tissue samples were fixed in 4 per centum paraformaldehyde for 24 hour, afterwards in 30 per centum sucrose at 4˚C, until these tissues sank. After embedded in embedding reagent for frozen sections, 6-μm sections were obtained onto polylysine-coated slides. These slides were treated with acetone at 4˚C for 15 min and then with PBS (phosphate buffered solution). After treatment with 0.5% Triton X-100 at 37˚C for 30 minute, sections were hatched with 10% normal goat serum for 45minute at 37˚C. Subsequently, these sections were treated with foremost antibody (PDGF-A: 1:200; vimentin: 1:2500) at 4˚C overnight and secondary antibody (FITC conjugated goat anti-mouse antibody: 1:200; rhodamine red conjugated goat anti-rabbit antibody: 1:200; DAPI: 1:2000) at 37˚C for 30 min. After washing in PBS 5 times (5 min for each), mounting was done with anti-quencher, and sections were observed under a fluorescence microscope and photographed (×200). ImageJ image analysis software was employed to analyze and merge these photographs. Negative controls were obtained by omitting the incubation with primary antibodies.

2.5. Detection the Expressions of mRNA of PDGF-A and Type I, III Collagen by RT PCR

In brief, frozen human right atrial tissue samples were thawed and homogenized on ice, then overall RNA was isolated using RNA-simple Total RNA Kit (Tiangen Biotechnology, China) according to the corporation's directions and quantified. Then, using ReverTra Ace qPCR RT Kit (Tiangen Biotechnology) and according to the manufacturer's instructions, RNA was reversely transcribed into cDNA successfully. Amplification of cDNA was done on thermal cycler (Applied Biosystems Step One Plus System). The volume of the reaction mixture was 20 μl, according to merchant description, amplification was executed successfully (SYBR® Premix Ex Taq™ II PCR kit and Applied Biosystems Step One Plus System). The reaction conditions are as follows: pre-denaturation for 30 second at 95˚C and 40 cycles of 95˚Cfor 5 second and 60˚C for 30 second. The melt curve was applied to define the specificity of products. The supporting software was applied to analysis the Ct value of products. According to the following formula: ΔCt = Cttarget gene − Ctinternal reference, the ΔCt was **Table 1** Oligonucleotide probes calculated in two groups, respectively. The relationship between the

CT value of the target gene and the copies of this gene is negative, consequently, with the increase of the ΔCt, the gene expression decreased. Then, $2^{-\Delta\Delta Ct}$ method was applied to calculate the relative mRNA expression of target genes. Oligonucleotide probes were in Table 1.

2.6. Western Blotting Analysis

For Western blot analysis, frozen human right atrial tissue samples were used for protein isolation. Protein extraction was followed by the instruction of the total protein extraction kit (Apply gen Technologies Inc, China). Proteins (10 μg) was isolated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and transferred to nitrocellulose membranes (Stratagene, USA) followed by staining with Ponceau S solution (Sigma, USA). The membranes were blocked with 5% non-fat dry milk and then explored rabbit polyclonal anti-human PDEGF-A (Abcam, USA) antibodies. Horse radish peroxidase-conjugated rabbit anti-mouse or anti-rabbit IgG (1:5000, Santa Cruz Biotechnology) was used as secondary anti-body followed by incubation with ECL Western Blot Detection Kit (Amersham, The Netherlands). The amount of protein chosen was in the linear immunoreactive signal range. The immunoreactive signals were exposed to Kodak film for 5 min and analyzed with gelpro analyzer after analysis software (Bio-Rad, USA) normalized by the corresponding value of β-actin. Experiments were repeated three times and the mean was scored.

2.7. Statistical Analysis

All statistical analysis was made by the SPSS version 15.0. If they were normally distributed, continuous variables were indicated as mean ± standard deviation (x ± s). Comparisons of means were applied to independent t test between AF group and SR group. Groups for categorical variables were analyzed by chi-square. Correlation coefficients were assessed between PDGF-A and LAD, including the protein and mRNA expression of PDGF-A. A value of $P < 0.05$ was considered statistically significant.

The reporting of this study conforms to STROBE guidelines.

Table 1. Oligonucleotide probes.

The target genes	Primers	Base composition
PDEGF-A	sense	5'-ACGTCCGCCAACTTCCTGA T-3'
	antisense	5'-TCCGGATTCAGGCTTGTGGT-3'
Type I collagen	sense	5'-GCGACAGAGGCATAAAGGGT-3'
	antisense	5'-CCAGGGAGACCGTTGAGTC-3'
Type III collagen	sense	5'-GAGCTTCCCAGAACATCA-3'
	antisense	5'-ATTCCCCAGTGTGTTTCG-3'
GAPDH	sense	5'-CCTCCTGCACCACCAACT-3'
	antisense	5'-CTTCTGGGTGGCAGTGATG-3'

3. Results

3.1. Clinical Characteristics

Patients' characteristics are shown in Table 2. As a whole, most characteristics were similar between two groups. Left and right atrial diameters, measured by echocardiography, were significantly larger in the AF group than the SR group. All drugs were stopped at least 12 h before surgery.

3.2. Collagen Content and Distribution

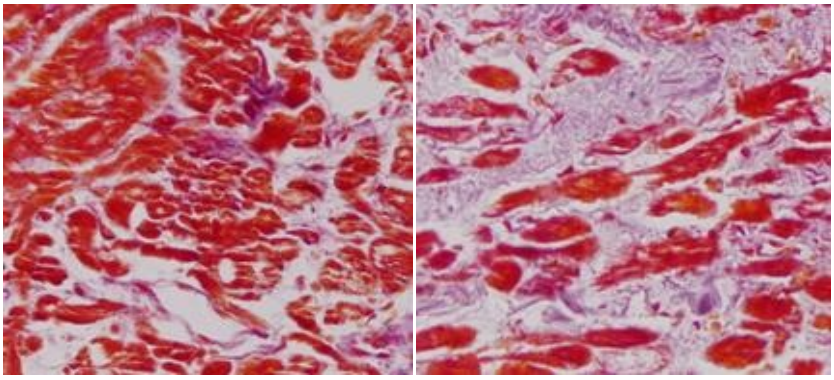
Representative examples of right atrial tissue stained with Masson's trichrome from each group are shown in Figure 1. Although the marked interstitial alterations were present because of all patients with RMVD, an apparent difference was observed between the two groups.

Comparison with the SR (Figure 1(a)) patients, there were abundant collagen fibers in the AF (Figure 1(b)) group. On the contrary, only a small amount of collagen fibers was observed in the SR group. The CVF in the AF patients (45.4% ± 2.33%) increased more drastically than that in the SR patients (12.9% ± 1.02%) ($P < 0.001$; Figure 1(c)), indicating some relationships between AF and fibrosis.

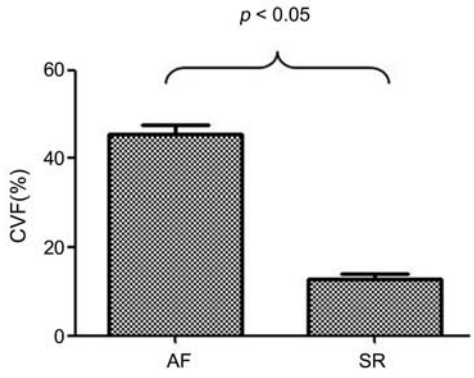
Table 2. Clinical characteristics.

	AF (n = 39)	SR (n = 45)	t/χ^2 values	P value
Basic data				
Age (years)	51.1 ± 9.0	48.1 ± 10.9	−1.405	0.164
Sex	24/15	19/26	3.083	0.086
male/female (n)				
SBP (mmHg)	112.4 ± 10.4	115.8 ± 14.3	1.242	0.218
DBP (mmHg)	71.7 ± 7.4	70.5 ± 11.5	−0.567	0.572
Laboratory examinations				
WBC (10^9/l)	6.29 ± 1.55	6.0 ± 1.91	−0.763	0.448
RBC (10^{12}/l)	4.55 ± 0.67	4.44 ± 0.51	−0.811	0.420
HB (g/l)	137.1 ± 16.6	135.3 ± 16.8	−0.482	0.631
CR (μmol/l)	92.47 ± 12.46	91.58 ± 12.43	−0.225	0.823
Echocardiographic parameters				
LVEF (%)	53.10 ± 5.90	54.47 ± 5.90	1.041	0.301
LAD (mm)	58.03 ± 13.93*	49.55 ± 17.17*	−2.420	0.018
RAD (mm)	26.88 ± 4.81*	24.32 ± 4.26*	1.721	0.038

SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; RBC, red blood cell; HB, hemoglobin; CR, serum creatinine; LVEF, left ventricular ejection fraction; LAD, left atrium diameter; RAD, right atrium diameter.



(a) (b)



(c)

Figure 1. Representative examples of right atrial tissue stained with Masson's trichrome. (a): the intensity of collagen fibers with Masson's Staining in SR (original magnification × 200). (b): the intensity of collagen fibers with Masson's Staining in AF (original magnification × 200). (c): CVF was higher in AF group. AF, atrial fibrillation; SR, sinus rhythm.

3.3. mRNA Expressions of Type I Collagen and Type III Collagen

We performed qRT-PCR to test whether the type I collagen or type III collagen level increases in the AF patient's right atrial tissues. After RT-PCR, the Ct value and number of cycles were applied to depiction, and finally, the mRNA's amplification curve was acquired. The results demonstrated that the way has good repeatability and consistent amplification efficiency. $2^{-\Delta\Delta Ct}$ method was applied to represent the relative expressions of target genes. The results displayed that the expression of mRNA of type I collagen was 2.042 ± 0.177 in the AF group, which was markedly higher than those in the SR group (0.988 ± 0.099), $P < 0.05$ (**Figure 2(a)**).

Compared with the SR group, the expression of type III collagen mRNA in the AF group was greater, but there was no marked difference between the AF group and SR group (1.228 ± 0.151 VS 1.067 ± 0.068, $P > 0.05$), (**Figure 2(b)**).

3.4. Increased PDGF-A Expression in the Right Atrial of Patients with AF

Representative sections of the immunofluorescent stained right atrial tissue from each group are shown in **Figure 3**. Although PDGF-A was expressed in both

groups, compared with the SR group, the level of the PDGF-A's protein was apparently higher in the right atrial myocardium of the AF group (Figure 4).

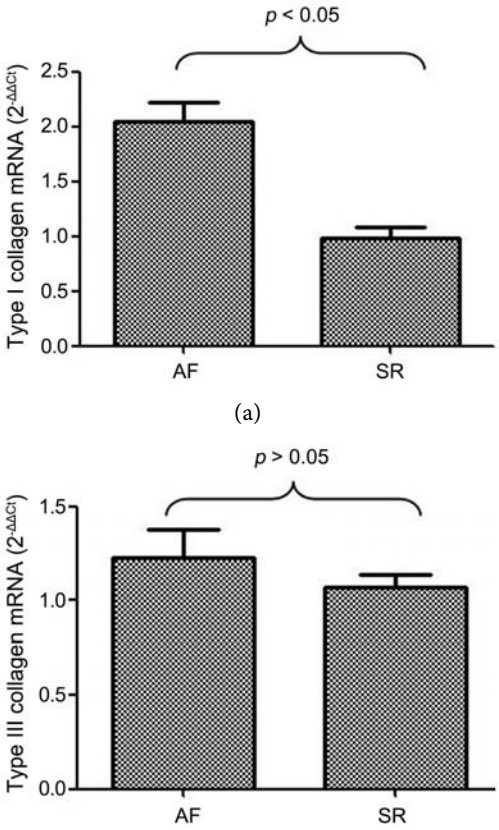
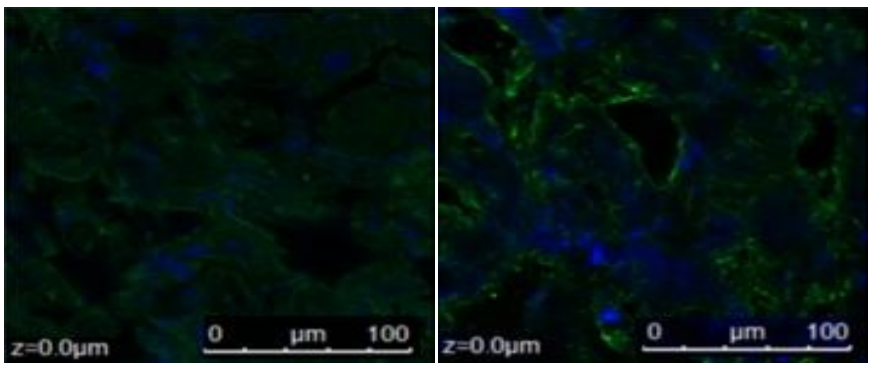


Figure 2. (a): mRNA expression of type I collagen in AF and SR groups; (b): mRNA expression of type III collagen in AF and SR groups. AF, atrial fibrillation; SR, sinus rhythm.



(a) (b)

Figure 3. Representative sections of the immunofluorescent stained right atrial tissue showed increased PDEGF-A in patients with AF compared with patients in SR. (a): Immunofluorescent stained expression of PDEGF-A in SR (original magnification × 200). (b): Immunofluorescent stained expression of PDEGF-A in AF (original magnification × 200). AF, atrial fibrillation; SR, sinus rhythm.

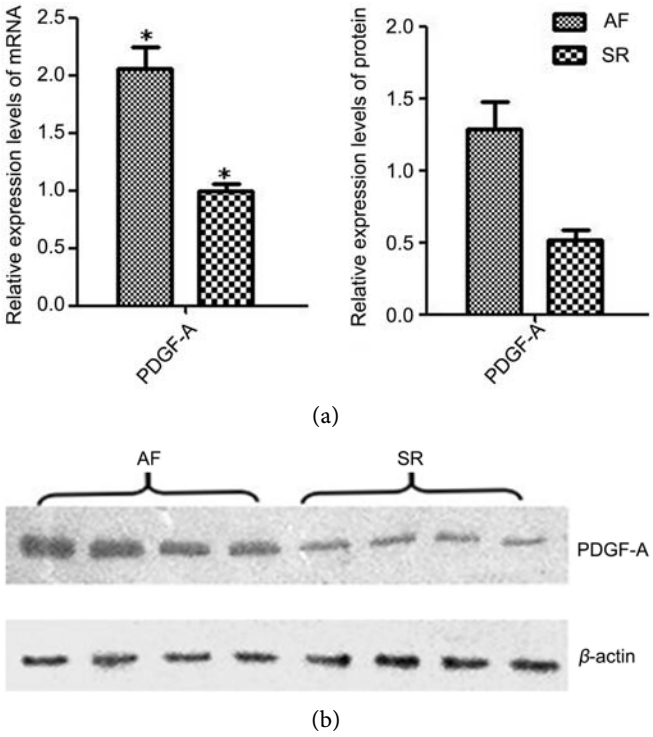


Figure 4. (a): Relative expression levels of mRNA and Protein in AF and SR groups; (b): Protein expression of PDGF-A in AF and SR groups by Western blotting; AF, atrial fibrillation; SR, sinus rhythm.

3.5. mRNA and Protein Expressions of PDGF-A

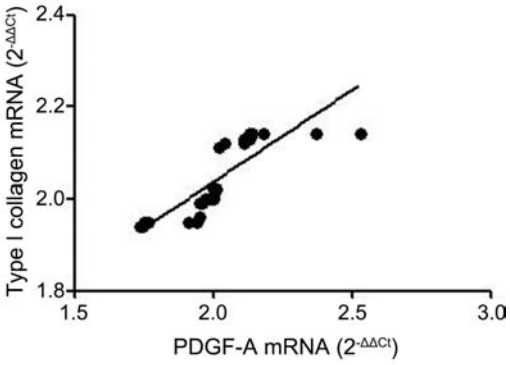
To test whether the PDGF-A increases in the right atrial tissues of the AF patients, we performed qRT-PCR and Western blotting. After real time PCR, the Ct value and number of cycles were applied to depiction, finally, the amplification curve of mRNA was acquired. The results demonstrated that the way has good repeatability and consistent amplification efficiency. $2^{-\Delta\Delta Ct}$ method was applied to indicates the relative expressions of target genes. The results displayed that the PDGF-A's mRNA expressions was 2.062 ± 0.184, the PDGF-A's protein expressions was 1.282 ± 0.193 in AF group, which were markedly higher than those in SR group (0.991 ± 0.062 and 0.517 ± 0.067, respectively; $P < 0.01$).

3.6. Positive Correlation between Protein and Gene Expression of PDGF-A and Type I Collagen

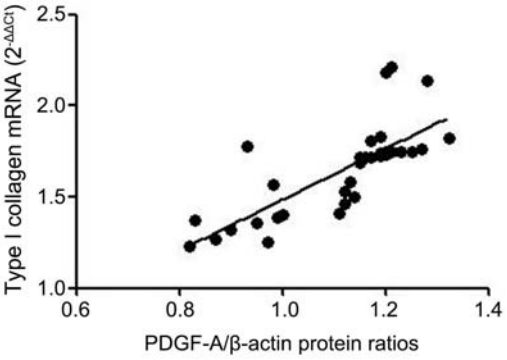
A strong positive correlation existed between mRNA of PDGF-A and Type I collagen; western blotting revealed a strong positive correlation between protein of PDGF-A and mRNA of Type I collagen (**Figure 5(a)**, $r = 0.75$; **Figure 5(b)**, $r = 0.72$, respectively).

4. Discussion

Numerous studies demonstrate that patients with chronic AF secondary to RMVD are very common, and in these patients, structural remodeling is very



(a)



(b)

Figure 5. (a): positive correlation existed between mRNA of PDGF-A and Type I collagen in AF group; (b): positive correlation between protein of PDGF-A and mRNA of Type I collagen in AF group; AF, atrial fibrillation.

important for AF initiation and maintenance [13] [14]. Atrial fibrosis, as a hallmark of structural remodeling, has been implicated in tissue biopsies from AF patients [15]. Atrial fibrosis results from extracellularmatrix (ECM) accumulation of fibrillar collagen deposits [16]. Interstitial fibroblasts are differentiated to myo fibroblasts, which produce large amounts of collagen that replace degenerating myocardial cells. Expansion of ECM between cardiomyocytes may cause conduction delays and create alternate conduction pathways. These changes result in ectopicfoci and anisotropic conduction, creating nonuniform wave fronts that facilitate abnormal reentrant arrhythmias. Atrial fibrosis involves multiple factors such as the rennin-angiotensin system, TGFβ1, oxidative stress and in fl ammation [17], but the exact mechanisms responsible for the structural changes that accompany AF in patients with RMVD are unknown. It is clear that atrial fibrosis occurs as a result of underlying cardiac disease (e.g. RMVD) affecting atrial tissue, and this process of remodeling in turn acts as a substrate for the initiation and maintenance of AF [18] [19].

Fibrosis is thought to occur on both a tissue and cellular level, and our study aimed to investigate the signaling pathways responsible for atrial fibrosis.

PDGF is mainly released by platelet α particles, in addition to monocytes, smooth muscle cells, endothelial cells, etc. can synthesize and release PDGF. PDGF is an important cell-stimulating agent that can stimulate the division and proliferation of a variety of cells, and has chemotaxis on fibroblasts and smooth muscle cells. About 85% of the extracellular matrix in normal myocardial tissue is composed of extracellular collagen secreted by fibroblasts, of which type I collagen accounts for about 85% and type III collagen accounts for about 11%.

PDGF-A is a potent growth factor that plays important roles in the proliferation [20], migration and survival of interstitial cells. An increasing number of proof has proved that PDGF/PDGFR signaling pathway is associated with the pathological fibrosis of multiple organs. PDGF and its receptor system play an important role in the development of myocardial fibrosis. In addition, during myocardial fibrosis in salt-sensitive hypertensive rats, PDGFR-α acts at early stage, and PDGFR-α expressions increase in fibroblasts and myofibroblasts, suggesting that PDGF/PDGFR signaling pathway is involved in the myocardial fibrosis via stimulating fibroblasts to proliferate and transform into myofibroblasts and to secret massive collagens [21] [22]. PDGF-α receptor mRNA is upregulated in acutely rejecting cardiac allografts, and mRNA of PDGF-A is upregulated in chronically rejecting cardiac allografts [23]. PDGF-A markedly increased pro fibrotic TGFβ-1 mRNA and accelerated the formation of myocardial fibrosis, indicating that PDGF may also increase TGFβ-1 levels to the formation of fibrosis. Atrial fibrillation, characterized by atrial fibrosis, is a frequent arrhythmia, which increases the risk of stroke and heart failure [24] [25]. Injection of neutralizing PDGFR-α specific antibody alleviated atrial fibrosis [26] [27]. The present research demonstrates that atrial fibrosis is distinct in patients with AF secondary to RMVD, establishing the relationship between PDGF-A and atrial fibrosis. This result strongly suggests that PGDF-A may be a good target for antifibrotic therapy in the heart.

But due to this study is a human tissue experiment, only right atrial tissue was collected, research data from left atrial tissue was missed. So it cannot simultaneously explore the relationship between PDGF-A and left atrial fibrosis in patients with atrial fibrillation secondary to RMVD, and therefore the distribution and expression of PDGF-A, the atrial structural remodeling cannot be contrasted between the left and right atria.

5. Conclusion

There was significant atrial remodeling in patients with chronic AF secondary to RMVD26; PDGF-A in patients with atrial fibrillation was highly expressed in the right atrial, and was closely related to atrial fibrosis. PDGF-A may be up-regulated expression of type I collagen gene, which participated into atrial fibrosis. Present study is a human tissue experiment, only right atrial tissue is collected. So it cannot simultaneously explore the relationship between PDGF-A and left atrial fibrosis in patients with atrial fibrillation secondary to RMVD.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Diagnostic Value and Safety of CT and US-Guided PTNB for Peripheral Pulmonary Lesions: A Meta-Analysis and Clinical Study

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Abstract

Objective: To evaluate the diagnostic value and safety of CT and ultrasound-guided PTNB for peripheral type of occupying lung lesions by meta-analysis and clinical study. **Methods**: 1) The target data of randomized controlled trials of CT and ultrasound-guided PTNB for peripheral type of occupying lung lesions were extracted by computer search of foreign PubMed, Embase, the Cochrane Library, Web of Science databases, since the establishment of the database. Cochrane quality assessment criteria were used for evaluation. Statistical analysis was performed using Review Manager 5.3 software. 2) To retrospectively study the diagnosis rate and complication rate of patients, undergoing CT or ultrasound-guided PTNB in the First Affiliated Hospital of Dali University from January 2015 to December 2020. **Results**: Meta-analysis included 7 papers with a total of 1177 patients including 502 patients in the ultrasound group and 675 patients in the CT group. Meta-analysis results showed that there was no difference in the diagnosis rate of PTNB guided by ultrasound and CT. The incidence of postoperative complications was higher in the CT group than in the ultrasound group. The incidence of postoperative pneumothorax was higher in the CT group than in the ultrasound group, and there was no difference in the incidence of postoperative bleeding. 3) Clinical study results show that the puncture success rate was 100% in both of the ultrasound and CT groups, the pathological diagnosis rate was 85.48% in the ultrasound group and 91.67% in the CT group, and there was no difference in the overall complication rate between the two puncture groups. **Conclusion**: Either ultrasound or CT-guided PTNB is a safe and effective clinical diagnostic method for the diagnosis of peripheral pulmonary occupations.

Keywords

Ultrasound, Computed Tomography, Percutaneous Lung Biopsy, Meta-Analysis, Retrospective Study

1. Introduction

The early stage of lung cancer mostly appears in the form of lung nodules, which are not clinically obvious and have a high underdiagnosis rate, and the extensive local invasiveness and distant metastasis are the reasons for the poor prognosis of lung cancer, therefore, early detection and diagnosis are important for the treatment of the disease [1] [2]. With the widespread use of low-dose computed tomography (LDCT) for lung cancer screening, the detection of peripheral pulmonary lesions (PPL) is increasing, and LDCT in high-risk groups can reduce the mortality rate of lung cancer by 20% [3] [4] [5]. Currently, pathological diagnosis is still the gold standard for lung cancer diagnosis, and more specimens are needed to evaluate targeted therapies based on the latest advances in EGFR, ROS1, gene PD-1 and other current lung cancer targeted therapies and immunotherapy. Surgical biopsy is a reliable method for diagnosing malignant disease and obtaining a sufficient volume of sample tissue, but the method is invasive. Bronchoscopy although a safe diagnostic method, has a rather low diagnostic yield for peri-pulmonary type lesions, with rates ranging from 46% to 88% [6] [7] [8] [9]. Percutaneous transthoracic needle biopsy (PTNB) is now an effective and safe minimally invasive technique for obtaining tissue samples from intrathoracic lesions, with ultrasound and CT being the two commonly used imaging-guided modalities [10]. The method is mainly used for peripheral lung lesions and pleural biopsies as well as central lung lesions, where pathological specimens cannot be obtained by bronchoscopy. Percutaneous lung biopsy provides tissue samples for diagnosis and staging and helps to differentiate primary cancer from distant metastatic or infectious lesions, which is essential for the proper treatment of lung lesions [11]. Percutaneous lung biopsy is also used to obtain tissue samples for genetic and immunological testing for cancer mutations, which can be used to determine radiotherapy regimens for patients undergoing targeted chemotherapy and to personalise treatments [12]. This technique is widely accepted and trusted, and previous studies have shown that percutaneous lung aspiration biopsy has a diagnostic efficacy of 98% for peripheral lung lesions, with a low complication rate, the technique has been accepted and trusted [13] [14].

There are two types of percutaneous lung puncture biopsy techniques, ultrasound and CT guidance, and the most common studies at home and abroad have mainly focused on single imaging-guided puncture, while relatively few studies have compared the two, and the small sample sizes of previous studies have been less convincing. This study will provide more scientific evidence on

the evidence on the early detection, diagnosis and treatment of peri-pulmonary lung cancer, mainly through meta-analysis and combined with clinical case studies.

2. Meta-Analysis of the Diagnostic Value and Safety of CT and US-Guided PTNB for Peripheral Pulmonary Space-Occupying Lesions

2.1. Literature Search Strategy

The computerized search was conducted for literature published in PubMed, Embase, The Cochrane Library, and Web of Science databases, since the establishment of the database, and the language of the literature was restricted to English. The search terms were ultrasound (US) computed tomography (CT) biopsy peripheral pulmonary lesions and ercutaneous lesions peripheral pulmonary lesions peripheral pulmonary nodules etc. The search terms took the form of mutual combinations of subject words and free words. The boolean logical operators AND, OR, and NOT were used for the combined search and adjusted accordingly to different databases, while all references included in the literature were checked and supplemented by manual search, in order to search all relevant literature as comprehensively as possible.

2.2. Data Extraction

Data extraction requires the participation of at least two researchers who read and screen the included literature according to the established inclusion and exclusion criteria respectively. The researchers then cross-check the screening results with each other. In case of disagreement, a consensus decision is made and the required data are entered into a pre-designed form. The main data extracted included the time of publication of the first author the characteristics of the study population (including number of cases gender age), and the outcome indicators of the intervention.

2.3. Evaluation of the Quality of the Literature

The risk of bias was assessed using the Cochrane Collaboration Network Evaluation of Risk of Bias tool, including randomized methods, allocation concealment, blinding, selective reporting bias, other bias, and completeness of data. A schematic diagram of the methodological quality assessment of the literature and the percentage of each quality assessment item were plotted using RevMan 5.3 software.

2.4. Publication Bias

A funnel plot was drawn using Review Manager 5.3 software and the risk of publication bias was considered to be low when the literature was roughly at the top of the funnel plot, and high when the literature was asymmetrically distributed or mostly at the bottom of the funnel plot.

2.5. Sensitivity Analysis

Included studies were removed one by one, and the change in effect values and heterogeneity before and after removal was observed to assess, whether each study would have an effect on the overall results. A study was considered heterogeneous if the heterogeneity changed after deletion of a study and the combined effect values remained statistically significant. The source of heterogeneity needs to be further analyzed, such as the sample size, the accuracy of the original data included in the study, the correct method of data extraction etc. If the combined effect values and changes in heterogeneity are not significant after item-by-item deletion, then it is said that the results of the study are reliable and robust.

2.6. Statistical Analysis

Meta-analysis was performed using RevMan 5.3 software. Risk Ratio (RR) and its 95% Confidence Interval (95% CI) were used as effect analysis statistics for categorical data, and Mean Deviation (MD) or Standardized Mean Difference (SMD) and its 95% CI were used as effect analysis statistics for quantitative data. Difference (MD) or standardized mean difference (SMD) and its 95% CI were used as effect analysis statistics for quantitative data. Heterogeneity between the results of the included studies was analysed using the Q test (test level set at α = 0.1) and the I^2 value. Higgins JP [15] *et al.* classified heterogeneity into three levels low medium and high, which were expressed as 25%, 50% and 75% of the I^2 value respectively. In the Cochrane systematic evaluation, as long as the I^2 value was not greater than 50%, the heterogeneity was acceptable. If $P > 0.05$ and $I^2 < 50\%$, there was no statistical heterogeneity among the studies, and after excluding the effect of significant clinical heterogeneity, a fixed-effects model was used for analysis, if $P \leq 0.05$ and $I^2 \geq 50\%$, there was statistical heterogeneity among the studies, and a random-effects model was used for analysis. The test level for meta-analysis was set at $\alpha = 0.05$.

3. Results

3.1. Literature Screening Results

A total of 362 documents were detected through the aforementioned search strategy, and 8 relevant documents were obtained by manual search, 280 relevant documents were obtained after manual removal of duplicates by the literature management software, 16 relevant documents were obtained after further reading of the titles and abstracts and excluding irrelevant documents such as case reports. Meta-analyses and reviews, these 16 documents were then read in full text and excluded from the study after further reading of the titles and abstracts, 16 relevant papers were obtained after excluding case reports, meta-analyses, reviews and other irrelevant literature [16]-[21]. The flow chart is shown in **Figure 1**.

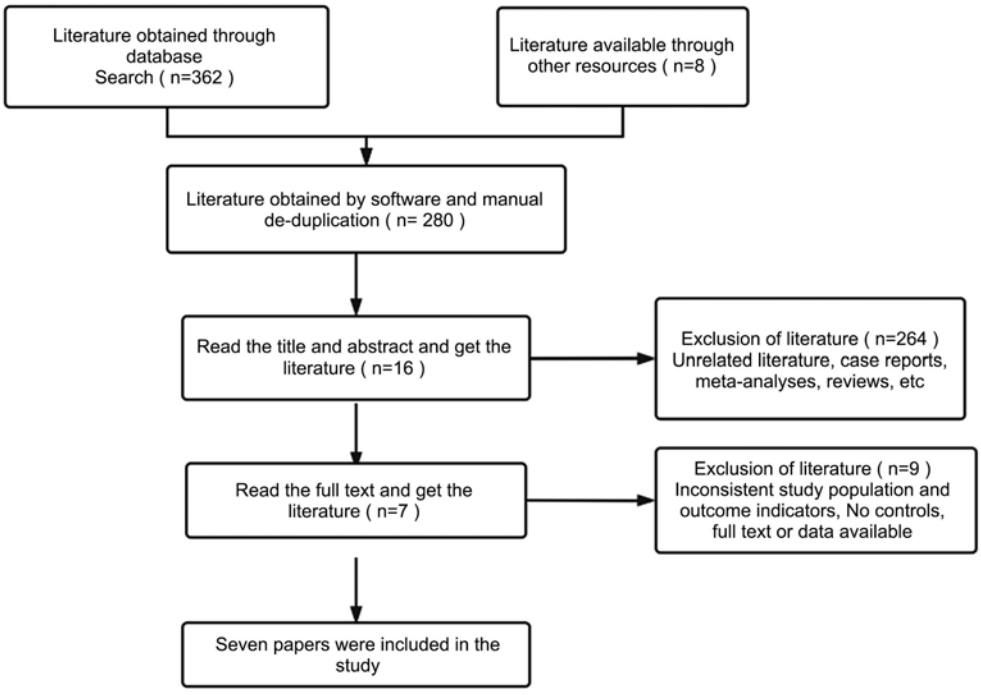

Figure 1. Flow chart of literature screening.

3.2. Basic Characteristics of the Included Literature

Seven randomised controlled trials with a total of 1177 patients were included in this study, including 502 patients in the ultrasound group and 675 patients in the CT group, the basic characteristics are shown in **Table 1**.

3.3. Methodological Assessment of the Included Literature

All included literature was assessed for risk bias according to the quality assessment methods for RCT literature provided in the Cochrane Handbook. See **Figure 2** for + for met, - for not met, and ? for unclear. The results suggest that most of the included literature was at low risk of bias, one literature indicated a high risk of assigning hidden methods and 5 did not explicitly state a specific allocation concealment method. One literature indicated a high risk of allocation concealment and five did not specify the specific allocation concealment method, three failed to specify the blinding method. All included literature had complete data results and no selective publication, 2 may have other biases [17] [18] [19] [20] [21]. The percentage of items included in the methodological assessment of the literature is shown in **Figure 3**.

3.4. Meta-Analysis Results

3.4.1. Forest Plot of Diagnostic Rates

All seven papers gave data on the rate of puncture diagnosis [16]-[21], with the rate of puncture diagnosis calculated for the ultrasound and CT groups, P = 0.02, I^2 = 60%, with some heterogeneity. A random effects model was used for the combined analysis and the meta-analysis showed no statistically significant

difference in puncture diagnosis rates between the two groups (RR = 1.03, 95% CI [0.99, 1.07], Z = 1.33, P = 0.18).See Figure 4 for details.

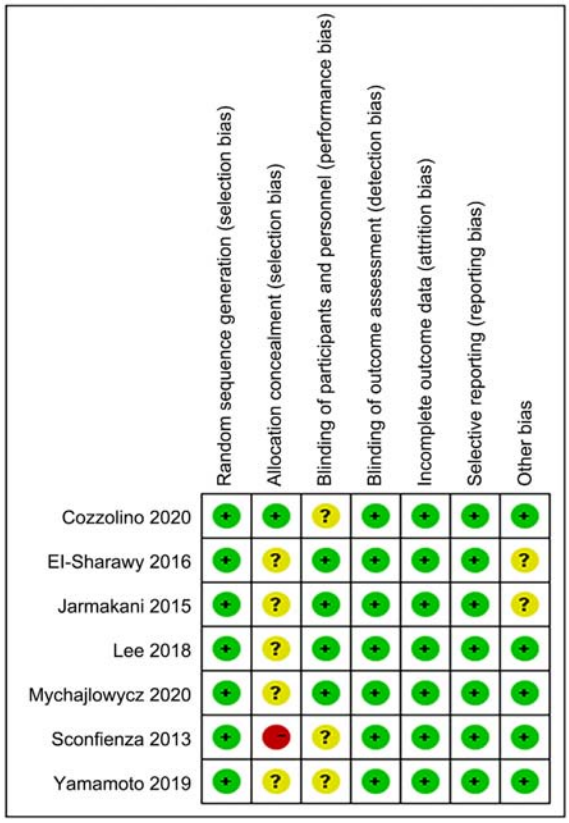

Figure 2. Methodological quality assessment of the included literature.

Table 1. Basic characteristics of the included literature.

Author	Year	Type of study	Number of cases (m/f)		Number of diagnoses		Complications of pneumothorax		Bleeding complications	
			Ultrasound group	CT Group	Ultrasound group	CT Group	Ultrasound group	CT Group	Ultrasound group	CT Group
Cozzolino	2020	Randomized control	28/12	28/12	38	39	1	9	2	4
El-Sharawy	2016	Randomized control	35/15	34/16	44	45	2	3	2	3
Jarmakani	2015	Randomized control	32/23	87/43	54	113	1	7	0	0
Lee	2018	Randomized control	78/72	60/40	147	93	10	21	0	0
Mychajlowycz	2020	Randomized control	22/21	54/61	42	114	5	17	1	8
Sconfienza	2013	Randomized control	44/59	71/99	100	164	6	25	1	2
Yamamoto	2019	Randomized control	49/12	54/16	57	59	0	12	2	5

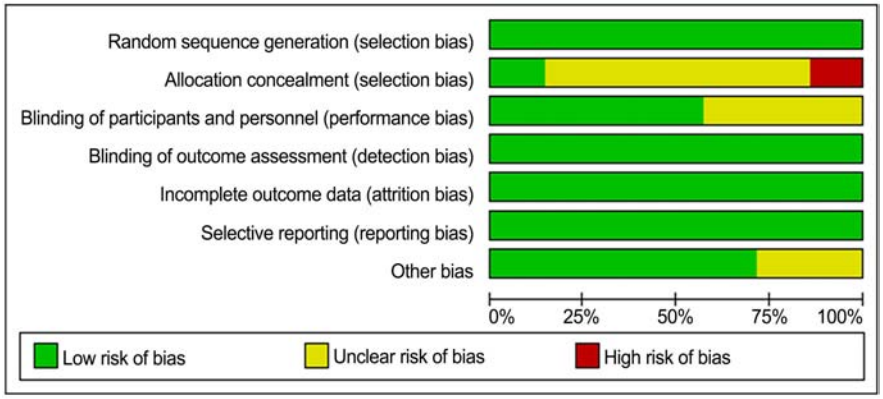

Figure 3. Percentage of items included in the methodological quality assessment of the literature.

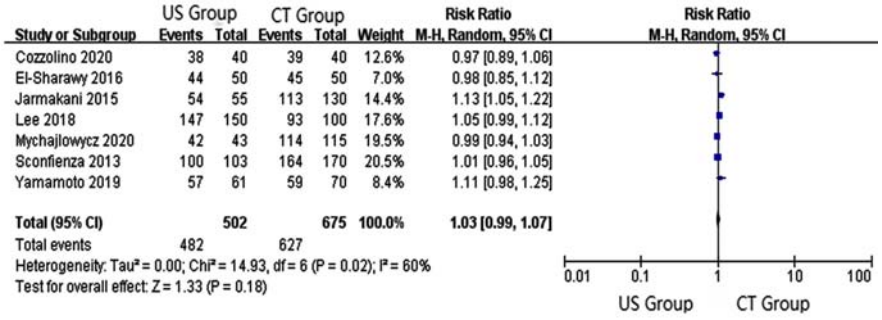

Figure 4. Diagnostic yield of CT and ultrasound-guided PTNB for peripulmonary space-occupying lesions.

3.4.2. Sensitivity Analysis of Diagnostic Rates

Sensitivity analysis was performed on the seven included papers due to the large variation in the included literature. By excluding one literature at a time, it was found that after excluding the Jarmakani group of the studies was significantly less heterogeneous, the results P = 0.22, I^2 = 29%, RR = 1.01, 95% CI [0.98, 1.05], Z = 0.69, P = 0.49, the conclusion was the same as the original results, therefore the meta-analysis of puncture diagnostic rates was more credible. See **Figure 5** for details.

3.4.3. Overall Complication Forest Map

All seven papers reported in detail on the complications studied [18] [19] [20] [21], mainly including data on the occurrence of haemorrhage and pneumothorax, none mentioned serious complications such as air embolism and death. The overall complication rate after puncture was used as a calculation, P = 0.48, I^2 = 0% and there was no heterogeneity in the included literature. A fixed effects model was used for the combined analysis and the results of the meta-analysis showed a statistically significant difference suggesting a total complication rate between the two groups (RR = 0.37, 95% CI [0.25, 0.53], Z = 5.36, P < 0.00001), indicating that the CT group had a higher postoperative complication rate than the ultrasound group. See **Figure 6** for details.

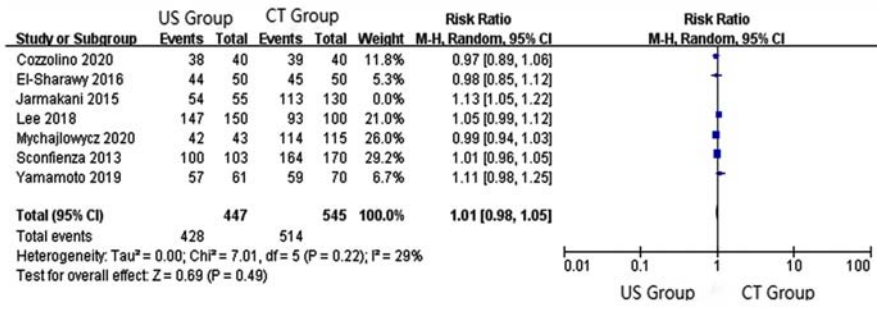

Figure 5. Diagnostic rates after excluding data from the Jarmakani group.

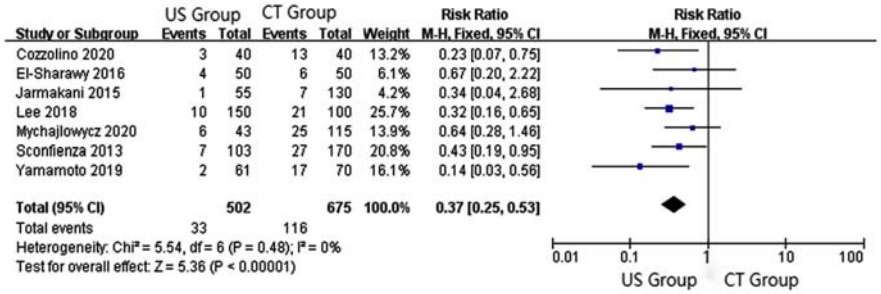

Figure 6. Total complication rate.

3.4.4. Forest Chart of Pneumothorax Complications

Pneumothorax was reported in all seven included papers [19] [20] [21], and most pneumothoraxes were self-resorbing, with only a minority of patients requiring postoperative closed chest drainage, the incidence of pneumothorax was used as a calculation, P = 0.33, I^2 = 14% and there was no heterogeneity in the included literature. A fixed-effects model was used for the combined analysis and the results of the meta-analysis showed a statistically significant difference suggesting the incidence of pneumothorax between the two groups (RR = 0.34, 95% CI [0.22, 0.52], Z = 5.04, P < 0.00001), indicating that the incidence of postoperative pneumothorax was higher in the CT group than in the ultrasound group. See Figure 7 for details.

3.4.5. Forest Chart of Bleeding Complications

Bleeding was not reported in only two of the seven included papers [20] [21], while the rest experienced bleeding, using the incidence of bleeding as the calculation index, P = 0.98, I^2 = 0%, there was no heterogeneity in the included papers. A fixed-effects model was used for the combined analysis, and meta-analysis showed no statistically significant difference in the incidence of bleeding between the two groups (RR = 0.50, 95% CI [0.22, 1.14], Z = 1.65, P = 0.10), and the incidence of bleeding after puncture was similar in both groups. See Figure 8 for details.

3.4.6. Publication Bias Analysis

As shown, no significant bias was observed after funnel plot analysis of the included studies. See Figure 9 for details.

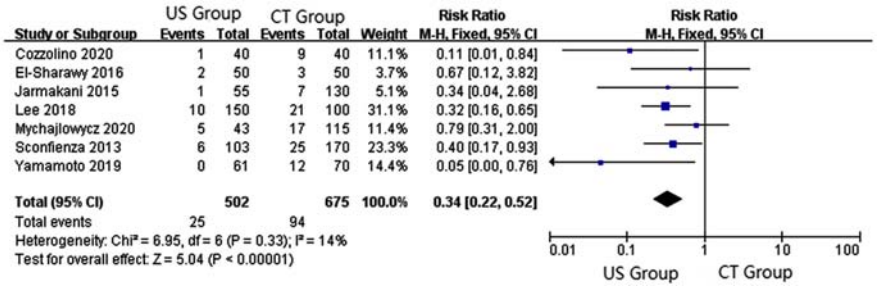

Figure 7. Incidence of pneumothorax.

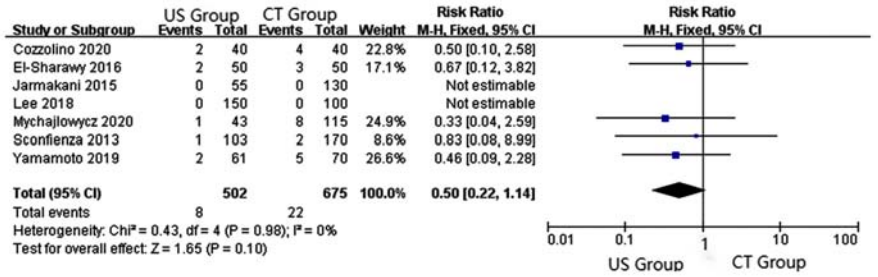

Figure 8. Incidence of haemorrhage.

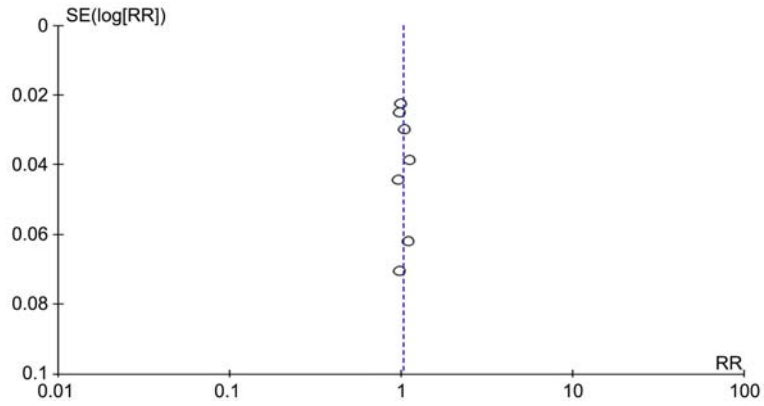

Figure 9. Funnel plot of puncture diagnostic rates.

4. Clinical Study on the Diagnostic Value and Safety of CT and US-Guided PTNB for Peripheral Pulmonary Space-Occupying Lesions

4.1. Research Content and Research Methodology

We retrospectively analyzed the general data, post-puncture complications, and pathological data of puncture materials of 110 patients to understand the diagnostic value and complications of ultrasound and CT-guided PTNB for peripheral type of occupying lung lesions.

4.2. Statistical Methods

All data were collated and analysed by the statistical software SPSS 26.0. The measurement data, expressed as mean ± standard deviation ($\overline{X} \pm S$), and count data were mainly expressed as composition ratio, count data were mainly based

on the magnitude of theoretical numbers. Pearson chi-square test, continuity-corrected chi-square test and fisher's exact probability method test were used. All tests were performed at $\alpha = 0.05$, and differences were considered statistically significant at $P < 0.05$.

5. Results

5.1. Puncture Success Rate and Complications

In both groups, percutaneous lung puncture was successful and the material was retrieved with a 100% puncture success rate.

Among the 110 patients, the overall complication rate in the ultrasound-guided group was 4.8%, including 3 (4.8%) cases of pneumothorax and no bleeding, the overall incidence in the CT-guided group was 16.7%, including 5 (10.4%) cases of pneumothorax and 3 (6.3%) cases of bleeding, none of the patients had serious complications, and the compressed lung area of all pneumothorax patients was less than 10%, and most of the bleeding was a small amount of blood in the sputum, no special treatment was required, and the symptoms basically improved after bed rest and oxygenation. None of the patients suffered from respiratory distress or death due to air embolism. There was no statistically significant difference between the two puncture groups in terms of overall complication rate ($\chi^2 = 2.994$, $P = 0.084 > 0.05$), incidence of pneumothorax ($\chi^2 = 0.558$, $P = 0.455 > 0.05$) and incidence of bleeding ($\chi^2 = 1.976$, $P = 0.160 > 0.05$). See Table 2.

5.2. Characteristics of Mass Distribution and Puncture Pathology Findings in the Study Population

In this study, the maximum diameter of the lung masses in the ultrasound-guided group was 5.14 ± 1.78 cm, with 28 right lung lesions and 34 left lung lesions. The maximum diameter of the lung mass in the group receiving CT guidance was 4.69 ± 1.84 cm, with 22 left lung lesions and 34 right lung lesions, there was no statistically significant difference between the diameter of the lesion ($P = 0.790 > 0.05$) and the location of the lesion ($P = 0.621 > 0.05$).

A total of 53 cases of ultrasound-guided PTNB were diagnosed, with a clear diagnosis rate of 85.48%, including 34 cases of malignant lesions, including 16 cases of adenocarcinoma of the lung, 13 cases of squamous lung cancer, 1 case of small cell lung cancer, 1 case of other types of lung cancer, 2 cases of metastatic cancer and 1 case of T-lymphoblastic lymphoma, 19 cases of benign lesions, including 7 cases of mechanized pneumonia, 7 cases of tuberculosis, 3 cases of pneumonia, 1 case of neurofibroma and 1 case of inflammatory, a total of 44 cases of CT-guided PTNB were diagnosed, with a clear diagnosis rate of 91.67%, including 30 cases of malignant lesions, including 19 cases of adenocarcinoma of the lung, 4 cases of squamous lung cancer, 4 cases of small cell lung cancer, 1 case of other types of lung cancer and 2 cases of metastatic cancer, 14 cases of benign lesions, including 3 cases of mechanized pneumonia, 6 cases of tubercu-

losis, 3 cases of pneumonia, 1 case of neurofibroma and 1 case of adenoma. There was no statistically significant difference in the rate of puncture pathology diagnosis between these two groups ($\chi^2 = 0.992$, P = 0.319 > 0.05).

Thirteen of the 110 patients still did not receive a definitive pathological diagnosis after PTNB examination, nine in the ultrasound group and four in the CT group, these patients were subsequently perfected with bronchial transcranial examination and pathological specimens were taken, and one case of adenocarcinoma of the lung and four cases of squamous carcinoma of the lung were diagnosed by pathology. See Table 3 for details.

Table 2. Incidence of complications with the two guidance methods.

	Ultrasound group	CT Group	*c*2	P-value
Total complications	3 (4.8)	8 (16.7)	2.994	0.084
Pneumothorax	3 (4.8)	5 (10.4)	0.558	0.455
Bleeding	0	3 (6.3)	1.976	0.160

Table 3. Specific puncture and pathology results.

Features	Ultrasound group (n = 62)	CT group (n = 48)
Longest diameter of lesion (cm)	5.14 ± 1.78	4.69 ± 1.84
Lesion location		
Left lung	28 (45.2)	22 (45.8)
Right lung	36 (54.8)	34 (54.2)
Pathological diagnosis of lesions		
Malignant lesions		
Adenocarcinoma	16 (25.8)	19 (39.6)
Squamous carcinoma	13 (20.1)	4 (8.3)
Small cell carcinoma	1 (1.6)	4 (8.3)
Other types of cancer	1 (1.6)	1 (2.1)
Metastatic cancer	2 (3.2)	2 (4.2)
T-lymphoblastic lymphoma	1 (1.6)	0 (0.0)
Benign lesions		
Mechanized pneumonia	7 (11.3)	3 (6.3)
Tuberculosis	7 (11.3)	6 (12.5)
Pneumonia	3 (4.8)	3 (6.3)
Neurofibroma	1 (1.6)	0 (0.0)
Pulmonary fungal infections	0 (0.0)	1 (2.1)
Inflammatory pseudotumour	1 (1.6)	0 (0.0)
Adenoma	0 (0.0)	1 (2.1)
Unspecified nature	9 (14.5)	4 (8.3)

6. Discussion

Seven studies were included in this study, which compared the diagnostic value and safety of the two imaging-guided modalities, this meta-analysis study showed that all included studies had 100% puncture success, and the difference between the two diagnostic rates [RR = 1.03, 95% CI [0.99, 1.07], P = 0.18] was not statistically significant, indicating that ultrasound and CT-guided PTNB are effective and feasible for peripheral pulmonary space-occupying lesions are both effective and feasible. In terms of safety, meta-analysis showed no statistically significant difference in complication rates for bleeding (RR = 0.50, 95% CI [0.22, 1.14], P = 0.10), overall complication rates (RR = 0.37, 95% CI [0.25, 0.53], P < 0.00001), pneumothorax complications (RR = 0.34, 95% CI [0.22, 0.52], P < 0.00001) were statistically significant, and although the overall postoperative complication rate was higher in the CT group than in the ultrasound group, particularly for pneumothorax, both had a high safety profile for use in the diagnosis of peripheral type of occupying lung lesions.

Although percutaneous lung aspiration biopsy is recognized as a well-established and safe, minimally invasive diagnostic technique, it is still not immune to damage and complications can occur to a greater or lesser extent, although serious complications are rare. Common complications of percutaneous lung aspiration biopsy include pneumothorax and haemorrhage, while needle tract dissemination of malignancy, pleural reaction, embolism and even death are relatively uncommon.

Pneumothorax was one of the common complications of percutaneous lung puncture biopsy, but all were small amounts of pneumothorax and none required closed chest drainage treatment, ultrasound was performed in four cases with a complication rate of 4.8%, which was similar to that reported in the literature [22]. In the current study, the mean diameter of the lesions in the CT group (4.69 ± 1.84 cm) was smaller than that in the ultrasound group (5.14 ± 1.78 cm), and the complications of pneumothorax were higher in the CT group than in the ultrasound group, which is in line with the findings of Yeow *et al.* [23]. Although the difference in overall pneumothoracic complications between the two was not statistically significant, the aforementioned meta-analysis showed that the complications in the CT group were significantly higher than those in the ultrasound group, so it is better to choose the appropriate guidance method according to the lesion in clinical operation to reduce pneumothoracic complications as much as possible.

Bleeding was another common complication in this study, second only to the incidence of pneumothorax, in this study, three patients (6.3%) in the CT group had bleeding, with no significant hemothorax or intrapulmonary haematoma present, while no bleeding occurred in the ultrasound group, which is similar to previous reports [24] [25]. The reason for less bleeding in the ultrasound group may be that the method allows for knowledge of the lesion and surrounding blood supply, and real-time dynamic observation, rational planning of the

needle route, and avoidance of rich blood supply areas as much as possible during puncture. In addition, for lesions with a rich blood supply or vascularity, it is essential to assess the patient's bleeding tendency by improving coagulation before the procedure.

In this study, a total of 110 patients underwent percutaneous lung puncture biopsy and pathology revealed a total of 64 patients (58.2%) with malignant lesions, early detection and diagnosis of lung occupations are essential to improve the prognosis of lung cancer patients [26]. The early detection and diagnosis of lung occlusions is essential to improve the prognosis of patients with lung cancer. In addition 39.4% of patients in the benign lesion group in this study were tuberculosis, which is similar to the study by Guo *et al.* [27]. According to the Global Tuberculosis Report 2020 published by the World Health Organization, China has the second highest burden of tuberculosis with about 889,000 new cases of tuberculosis and 14% of patients, who are resistant to tuberculosis drugs in 2019, out of about 10 million new cases of tuberculosis worldwide [28]. The number of new cases of tuberculosis in China is about 880,000 and the proportion of patients with drug-resistant tuberculosis is 14, making it one of the countries with the highest burden of tuberculosis, tuberculosis is a major threat to human health and has become a global public health problem, so early diagnosis is important. The present results also confirm that ultrasound or CT-guided percutaneous puncture biopsy is one of the methods used to diagnose tuberculosis.

The mean diameter of the lesions in the ultrasound group in this study was 5.14 ± 1.78 cm, which was greater than the mean diameter of the lesions in the CT group (4.69 ± 1.84 cm). It has been noted that lesion diameter size has a significant impact on the diagnostic rate, with lesions larger than 5 cm in diameter having a 29% probability of liquefied necrotic areas in peripheral type lung occupancies, resulting in a lower pathological diagnosis rate [29]. CT can distinguish areas of liquefaction and necrosis based on the CT value of the lesion, avoiding the need for puncture in these areas, which ultrasound lacks [30]. Ultrasound lacks this advantage. For small lesions, the smaller the lesion, the more difficult it is to insert the needle accurately, the weak movements or erratic breath-holding during biopsy affects the accurate localisation of the lesion, and it is more likely that the sample will be obtained from the peripheral area of the lesion rather than from the lesion itself [31]. However, there is a small group of people who believe that the size of the lesion does not seem to affect the diagnostic yield of ultrasound-guided biopsy, because the operation allows the needle tip to be displayed in real time on colour doppler images, large vascular structures can be easily displayed to avoid injury, ultrasound allows real-time monitoring of the accompanying.

Lesion movement is with breathing [32]. Therefore, before performing the procedure, the size of the lesion needs to be assessed and the appropriate guidance modality selected to improve the pathological diagnosis. In summary, PTNB guided by either ultrasound or CT is a safe and effective clinical diagnos-

tic method for the diagnosis of peripheral pulmonary occupations. Depending on the actual condition of the patient and the lesion, choosing the appropriate guidance modality will not only improve the pathological diagnosis rate, but also reduce the occurrence of complications.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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The Impact of Electronic Cigarettes (e-Cigs) Smoking Habit on Periodontal Status and Salivary pH among Some Passive e-Cigs Smokers Referred to the College of Dentistry Clinics, King Khalid University

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Abstract

Background: Electronic cigarette (e-cigs) smoking is substitutional to traditional cigarette smoking to reduce the dangerous combustion of products. Moreover, passive smoking is involuntarily tobacco smoking due to the exposure to cigarette or tobacco smoke among non-smokers and due to there being little knowledge about the impact of passive e-cigs smoking on periodontal status and salivary pH. Therefore, the present study aimed to evaluate the effect of e-cigs smoking habit on periodontal tissue and salivary pH among some passive e-cigs smokers referred to the college of dentistry clinics, King Khalid University. **Material and Methods**: Ninety male participants who were referred to the college of dentistry clinics at King Khalid University were included in the study. Age, gender, e-cigs smoking, and general health were recorded. The participants were divided into three equal groups (n = 30) as follows: Group I (Non-passive e-cigs smokers and non-smokers) as the control group, Group II (e-cigs users), and Group III (Passive e-cigs smokers). Salivary pH, plaque control record (PCR), gingival bleeding index (GBI), clinical attachment loss (CAL), percentage of radiographic bone loss (% RBL), periodontal pocket depth (PPD), more than 5 missing teeth due to periodontal diseases (>5 MTDP), tooth mobility (TM), furcation involvement (FI), Bite collapse (BC), and less than 20 remaining teeth (10 Opposing pairs) (L20RT) as well as HbA1c were recorded. ANOVA test was used to the comparison between Groups I, II, and III in the participants' ages and periodontitis staging clinical findings. The mean of participants' age groups, the mean of

salivary pH values of study groups, and the periodontitis staging complexity and HbA1c were compared between groups with the ANOVA test, Tukey's test, and the chi-square test. P-value was recorded, and less than 0.5 was considered a statistically significant difference ($p < 0.5$). **Results**: The e-cigs users group revealed higher means of PCR, GBI %RBL values, and the participants percentages of >5 MTDP, TM, FI, L20RT, and diabetes mellitus (DM) among participants compared to the passive e-cigs smokers group and control group except for the participants percentage of BC among the participants, which was higher among the control group participants. The differences were not significant in PCR, GBI, %RBL and DM ($p > 0.5$) and significant in >5 MTDP, TM, FI, L20RT and smoking ($p < 0.05$). The passive e-cigs users group showed higher means of CAL, PPD, salivary pH values as well as the participants percentages of HbA1c > 7% values compared to the e-cigs users group and control group participants. The differences were not significant in CAL and PPD ($p > 0.5$) and significant in the participants percentages of salivary pH values ($p < 0.05$). **Conclusion**: The e-cigs smoking habit was the cause of an increase in periodontal disease severity among the electronic smokers rather than passive e-cigs smokers, although the salivary pH was higher in the latter.

Keywords

Electronic Smoking Habit, King Khalid University, Passive e-Cigs Smokers, Periodontal Status, Salivary pH

1. Introduction

The periodontal supporting tissues comprise gingiva, periodontal ligament, alveolar bone, and cementum which support the teeth and can help in the clinical assessment of oral health status [1]. Periodontal inflammatory disease is a widespread chronic disease in oral mucosa due to microbial dental plaque [2] [3] [4]. It is thought that some periodontal bacteria can initiate periodontal diseases and consider the main cause of missing teeth among the global people [5].

Smoking is a significant risk factor for the advancement of periodontal disease [6] [7]. Recently studies confirmed a potent link between smoking and worse periodontal status, an increase in dental plaque and calculus formation among smokers [8] [9] [10], causing harmful alteration in the oral microbiota, an inflammatory reaction, reducing the immune defense, consequently an increase in bone loss [11] [12] [13] [14]. Moreover, tobacco-containing outputs may be led to oral abnormal changes, such as leukoplakia, gingivitis, candidiasis, nicotine stomatitis, periodontitis, failure of surgical and prosthetic treatments, and a rise in the incidence of the oral malignant tumors [15] [16] [17]. Recently, there is a decrease in the smoking of classical cigarettes with the increase in the use of new tobacco products, such as electronic cigarettes [18].

The e-cigs is a mobile device based on battery-operated where its tank con-

tains three main liquid components: a transportersolution (propylene glycol or vegetable glycerin), nicotine (unless without nicotine), and favoring; which are heated by a resistor liberating an aerosol and breathed by the user during smoking [10]. The ingredients of e-cigs are controlled by the FDA as planning for smoking discontinuation or a less damaging replacement smoking for traditional cigarette smoking [19] [20]. The transition from traditional cigarette smoking to e-cigs decreases the number of cigarettes smoked without quitting smoking, and the risk effect of cigarette smoking on oral diseases remains a high probability [21] [22]. Some studies have revealed that smokers using e-cigs have the poor periodontal status [23] [24] [25].

Environmental tobacco smoke (passive smoking) exposure may be a risk factor for several systemic diseases in society [26]. There is an association between periodontal diseases in non-smokers and passive smoking, and passive smokers were affected 1.6 times more by the periodontal disease compared to those non-smokers, according to the clinical findings of Arbes *et al.*'s study [27] [28].

Saliva fluid has a significant role in preserving oral health by pH levels adaption and interfering with dental mineralization and periodontal health [29] [30]. The alteration in some characteristics of saliva can lead to abnormal changes in the oral environment, causing plaque and calculus formation as risk factors for gingivitis and periodontitis [31]. Some studies revealed that when the saliva is at a neutral or more alkaline pH, the healing of periodontal tissues improves, whereas a lower alkaline pH level might have a necrotizing effect on the periodontal tissues [32]. On the other hand, there is an association between the period time of smoking and salivary pH values according to the clinical findings of Parvinen T. study where he found that the levels of salivary pH rise during the first time of smoking periods and decrease with continuous smoking [33]. Even though many studies reported that e-cigs smoking has an impact on periodontal status and salivary pH values but the impact of passive e-cigs smoking on periodontal tissues and salivary pH and their relationship to the severity of periodontal diseases among referred participants to the college of dentistry clinics, King Khalid University is unknown. Therefore, we aimed to evaluate the periodontal parameters and the salivary pH values in e-cigs smokers, passive e-cigs smokers, and non-smokers based on the period time of smoking to clarify their relationship with periodontal status.

2. Materials and Methods

2.1. Study Design and Sample Size

This cross-sectional study was carried out between March 2022 and June 2022. The sample size for the study was 90 participants aged between 18 and 80 years who visited as outpatients in the college of dentistry, King Khalid University, Abha, Saudi Arabia. The patients were divided into 3 equal groups (n = 30): Group I as the control group (non-passive e-cigs smokers and non-smokers), Group II (e-cigs users), and Group III (passive e-cigs smokers). A predictive formula (Kang *et al.*, 2008) was applied in the assessment of the sample size of

the current study [34].

Data were collected by clinical interview and a periodontal examination. The clinical interview comprised questions about patients' characteristics, socioeconomic, medical/dental history and health, and attitudes, such as smoking. The glycated hemoglobin (HbA1c) of participants was recorded based on the medical reports in their files. The patients responded to questions about their data, systemic status, e-cigs smoking habit, and environmental smoking. Patients were divided according to their e-cigs smoking history into e-cigs smokers, passive e-cigs smokers, and non-smokers. The non-smoking group included the patients who confirmed that they had never smoked. The smoking group consisted of all patients who used e-cigs regularly every day for a year or more. All participants were in attendance, with the remaining at least 20 teeth.

2.2. The Inclusion and Exclusion Criteria

The inclusion criteria consisted: The male participants are regular e-cigs smokers every day for a year or more, the passive e-cigs male smokers every day for a year or more, the male participants who are at least 18 years of age, the male participants who have agreed to participate in the study and signed the patient's informed consent, the participants who are in good systemic healthy, and the participants who are not subjecting any medical therapy and any periodontal therapy in the past 6months. The exclusion criteria consisted: the participants who received medical therapy within the previous 6 months, irregular e-cigs smoking smokers who reported e-cigs smoking at some times or used e-cigs regularly every day for less than one year, irregular passive e-cigs smokers or passive e-cigs smokers less than one year, use of any complement vitamins nutrition, the participants who are with oral cancer, the participants who with oral lesions due to e-cigs smoking and had received medications, chemotherapy, or radiation therapy that caused dry mouth, the participants who are with systemic conditions which impact the salivary pH, the participants who are under drug therapy which impacts the salivary pH, the participants who had received periodontal therapy six months before the study, the participants who are with xerostomia, and the participants who are with completely edentulous ridges.

2.3. Ethical Statement

Ethical approval and ethical clearance certificate from the institutional review board of King Khalid University College of dentistry (IRB/KKUCOD/ETH/2021-22/045) were gained. This study was carried out according to the Declaration of Helsinki. The participants were separately informed about the objective of the study. All participants signed informed written consent before the study. The participants obtained all information details before starting the study. The treatment of participants' oral lesions was done with the right specialists.

2.4. Periodontal Status Assessment

The oral hygiene and gingival status assessment was done in outpatient clinics at

the college of dentistry, King Khalid University, and included dental plaque, gingival bleeding on probing, and periodontal tissues assessments. The following periodontal parameters were recorded: plaque control record (PCR) [35]; gingival bleeding index (GBI) [36]. The periodontal status was assessed by applying the guidelines of the 2017 World Workshop on periodontal diseases and conditions through recording the following clinical parameters: clinical attachment loss (CAL); percentage of radiographic bone loss (% RBL); periodontal pocket depth (PPD); more than 5 missing teeth due periodontal diseases (>5 MTDP); tooth mobility (TM); furcation Involvement (FI), bite collapse (BC), and less than 20 remaining teeth (10 Opposing pairs) (L20RT) [37].

2.5. Salivary pH Assessment

Saliva samples were obtained from the participants. Un-stimulated saliva was collected before the periodontal examination and after asking the participants to wash their mouths with water to remove the food debris or other materials. The samples were collected after 1 - 2 min for water clearance at least one hour after the last meal where each participant spit saliva into a sterile lab tube until 5 ml, then the salivary pH was recorded by using pH indicator strips [Dental Saliva pH indicator strips pH 6.5 - 9.0; gradation 0.5; color coded].

2.6. Statistical Analysis

The mean and standard deviation of participants' ages, periodontal disease staging clinical findings, and salivary pH values in the current study groups were calculated using the ANOVA test and Tukey's test. The periodontitis staging complexity clinical findings and periodontitis grading modalities among study groups were compared through the Chi-square test; on the other hand, the salivary pH among the three groups was compared to age, plaque control record, gingival bleeding index, clinical attachment loss, percentage of radiographic bone loss, and periodontal pocket depth by evaluating the correlations. A p-value of less than 0.05 was considered statistically significant ($p < 0.05$).

3. Results

According to the clinical findings, the current study evaluated the periodontal status and salivary pH values in three different groups of participants depending on the e-cigs smoking status. Table 1 and Figure 1 reveal the mean and standard deviation (±SD) of the age of participants included in the present study. The mean ages were recorded to be 32.3 ± 14.07 years old in Group I, 34.1 ± 8.84 years old in Group II, and 31.7 ± 5.5 years old in Group III. The table of participants' ages did not show any statistically significant differences in the comparison between Groups I, II, and III ($p > 0.5$). The values of salivary pH in the three groups were recorded in Table 2 and Figure 2. The mean salivary pH values in Group III (6.8 ± 0.12) were higher than the mean values recorded in Group I (6.7 ± 0.161) and Group II (6.3 ± 0.072). A highly statistically significant differ-

ence link was detected between e-cigs smoking habit, passive e-cigs smokers, and salivary pH values according to the use of ANOVA test in the comparison between Groups I, II, and III ($p < 0.001$) as well as in the comparison between Groups I and II ($p < 0.001$), Groups I and III (0.026) and Groups II and III ($p < 0.001$) according to Tukey's test. Table 3 and Figure 3(a) & Figure 3(b) exhibit the clinical findings of periodontal disease staging of Groups I, II, and III. The three groups correspond in the effect of e-cigs smoking habit and passive e-cigs smoking on the clinical findings of periodontal disease staging. Regarding PCR, gingival GBI, and % RBL, there were higher in these clinical findings values among the participants in Group II (68.03 ± 27.23, 73.4 ± 21.6, 44.17 ± 19.1, respectively) without statistically significant differences compared to Group III and I that having a lower mean of PCR (58.1 ± 25.7, 57.1 ± 23.5, respectively), GBI (61.1 ± 26.8, 68.9 ± 23.01, respectively) and % RBL (40 ± 16.1, 20.5 ± 10.6, respectively) ($p > 0.05$). In contrast, Group III had mean values of CAL (3.3 ± 3.2) and PPD (3.13 ± 0.9) higher than Groups I (3.2 ± 1.5, 2.9 ± 0.8, respectively) and II (3.1 ± 2.2, 2.6 ± 1.1, respectively) also without statistically significant differences ($p > 0.05$).

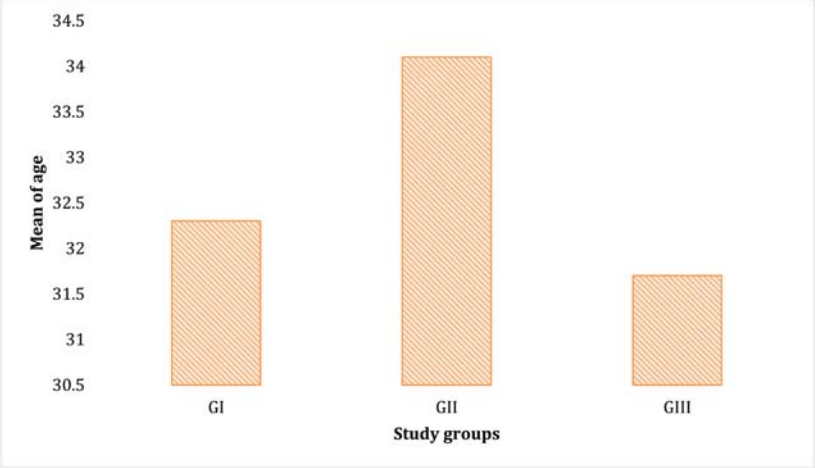


Figure 1. The mean ages of study groups. G: Group.

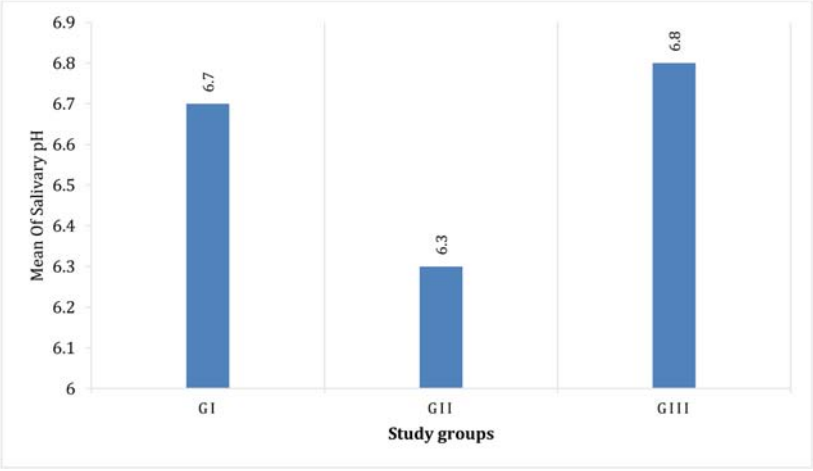


Figure 2. The mean of salivary pH values of study' groups. G: Group.

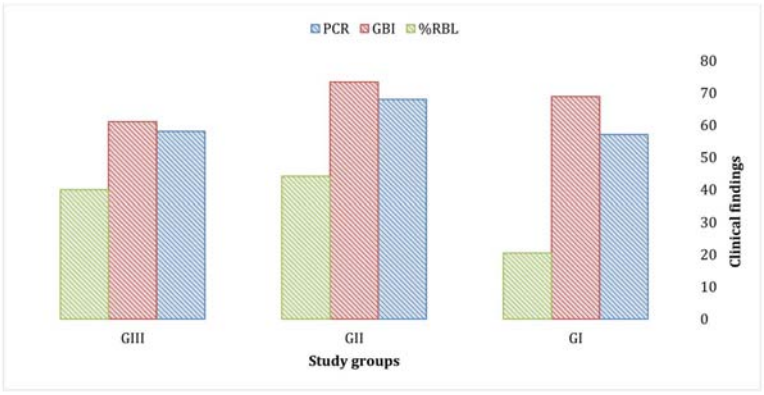
Table 1. Mean and standard deviation of ages study groups.

	Age			ANOVA	
	Group I	**Group II**	**Group III**	**F**	**p-value**
Range	18 - 80	20 - 53	25 - 50	0.459	0.634
Mean ± SD	32.3 ± 14.07	34.1 ± 8.84	31.7 ± 5.5		

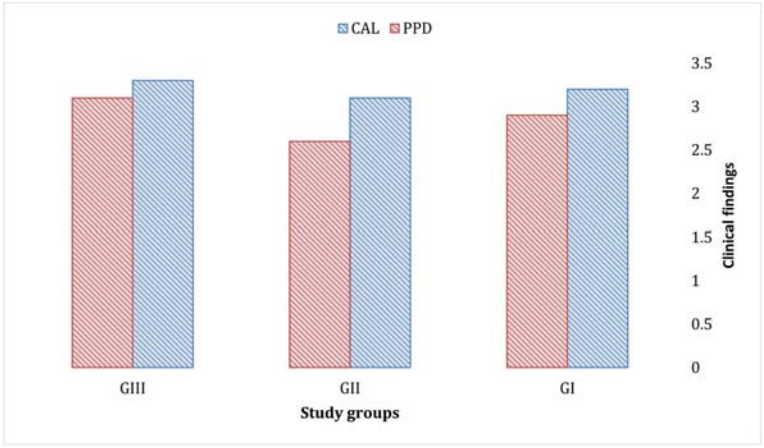
Table 2. Mean and standard deviation of salivary pH of study's groups.

	Salivary pH			ANOVA	
	Group I	**Group II**	**Group III**	**F**	**p-value**
Range	6.5 - 7	6.2 - 6.5	6.6 - 7.2	142.545	<0.001**
Mean ± SD	6.7 ± 0.161	6.3 ± 0.072	6.8 ± 0.12		
Tukey's test					
Group I & Group II		**Group I & Group III**		**Group II & Group II**	
<0.001**		0.026*		<0.001**	

* Significant difference between three groups at p-value less than 0.05, ** highly statistical significant difference between three groups.



(a)



(b)

Figure 3. (a) The clinical parameters of periodontal diseases staging. G: Group, PCR: Plaque control record, GBI: Gingival bleeding index, % RBL: Percentage of radiographic bone loss; (b) The clinical parameters of periodontitis staging G: Group, CAL: Clinical attachment loss, PPD: Periodontal pocket depth.

Table 3. Mean and standard deviation of periodontal disease staging clinical findings.

Items		Groups			ANOVA	
		Group I	Group II	Group III	F	p-value
PCR	Range	15 - 100	10 - 100	10 - 100	1.673	0.194
	Mean ± SD	57.1 ± 23.5	68.03 ± 27.23	58.1 ± 25.7		
GBI	Range	20 - 100	27 - 100	10 - 100	2.039	0.136
	Mean ± SD	68.9 ± 23.01	73.4 ± 21.6	61.1 ± 26.8		
CAL	Range	1 - 5	1 - 8	1 - 7	0.019	0.981
	Mean ± SD	3.2 ± 1.5	3.1 ± 2.2	3.3 ± 3.2		
% RBL	Range	2 - 50	15 - 60	10 - 40	1.771	0.231
	Mean ± SD	20.5 ± 10.6	44.17 ± 19.1	40 ± 16.1		
PPD	Range	1 - 5.6	1 - 4	1 - 5	1.833	0.170
	Mean ± SD	2.9 ± 0.8	2.6 ± 1.1	3.13 ± 0.9		

PCR: Plaque control record, GBI: Gingival bleeding index, CAL: Clinical attachment loss, % RBL: Percentage of radiographic bone loss, PPD: Periodontal pocket depth.

Regarding the clinical findings of periodontitis staging complexity in Table 4 and Figure 4, the e-cigs users group revealed the highest values in the participants' percentage affected with >5 MTDP (33.3%), TM (63.3%), FI (40%) and L20RT (10 Opposing pairs) (36.7%), whereas BC revealed the highest values in the participants' percentage affected (16.7%) among the participants of the control group. There were significant differences in the participants' distribution according to periodontitis staging complexity in the comparison between Groups I, II, and III ($p < 0.05$). The participants' distribution according to some periodontitis grading modalities was summarized in Table 5 and Figure 5. The percentage of participants who distributed of HbA1c test by more than 7% (33.3%) among Group III was higher than Group I (8.3%) and Group II (7.1%) without present statistical significance differences ($p > 0.05$). The correlation analysis in Table 6 indicated no significant and positive correlations between salivary pH and CAL and PPD. Moreover, salivary pH values revealed no significant and negative correlations with participants' ages, PCR, GBI, and % RBL.

4. Discussion

The e-cigs is a new device therapy for cigarette smoking by evaporating flavoring agents, nicotine, and propylene glycol as a smoking cessation method; but several studies could not confirm the efficacy of this method to complete stopping traditional cigarette smoking [38] [39] [40] [41] [42]. Several studies in Saudi Arabia were carried out on conventional tobacco products' effects on oral hygiene, but there is a shortage of studies that reveal the impacts of e-cigs smoking habit and passive e-cigs smoking on periodontal tissues and salivary pH values. Therefore, we carried out this study among referred patients to the college of dentistry clinics, King Khalid University, to compare e-cigs users with passive e-cigs smokers and nonsmokers to evaluate the effect of e-cigs smoking and passive e-cigs smoking on periodontal health status and salivary pH.

Table 4. The participants' distribution according to periodontitis staging complexity.

		Groups			Chi-square	
		Group I n(%)	Group II n(%)	Group III n(%)	X^2	p-value
>5 MTDP	N	24 (80.0%)	20 (66.7%)	29 (96.7%)	10.246	0.006*
	P	6 (20.0%)	10 (33.3%)	1 (3.3%)		
TM	N	20 (66.7%)	11 (36.7%)	21 (70.0%)	14.527	0.024*
	P	10 (33.3%)	19 (63.3%)	9 (30%)		
FI	N	28 (93.3%)	18 (60.0%)	29 (96.7%)	19.818	0.003*
	P	2 (6.7%)	12 (40%)	1 (3.3%)		
BC	N	25 (83.3%	29 (96.7%)	29 (96.7%)	9.181	0.05*
	P	5 (16.7%)	1 (3.3%)	1 (3.3%)		
L20RT	N	26 (86.7%)	19 (63.3%)	30 (100%)	18.111	<0.001**
	P	4 (13.3%)	11 (36.7%)	0 (0.0%)		

* Significant difference between three groups at p-value less than 0.05, ** highly statistical significant difference between three groups, >5 MTDP: More than 5 missing teeth due perio. Diseases, TM: Tooth mobility, FI: Furcation involvement, BC: Bite collapse, L20RT: Less than 20 remaining teeth (10 Opposing pairs), P: Positive, N: Negative, n: Number.

Table 5. The participants' distribution according to some periodontitis grading modalities.

		Groups			Chi-square	
		Group I n(%)	Group II n(%)	Group III n(%)	X^2	p-value
DM	N	18 (60%)	16 (53.3%)	21 (70.0%)	1.797	0.407
	P	12 (40%)	14 (46.7%)	9 (30%)		
HbA1c	<7%	11 (91.7%)	13 (92.9%)	6 (66.7%)	3.162	0.206
	>7%	1 (8.3%)	1 (7.1%)	3 (33.3%)		

DM: Diabetes Mellitus, HbA1c: Glycated hemoglobin, n = Number, P: Positive, N: Negative.

Table 6. The correlations between participants' ages and some clinical findings of periodontitis severity and salivary pH.

Correlations	Salivary pH.	
	r	p-value
Age	−0.100	0.348
Plaque control record PCR±	−0.127	0.236
Ginival bleeding index	−0.113	0.292
Clinical attachment loss CALL	0.073	0.702
% of radiographic bone loss	−0.547	0.081
Periodontal pocket depth	0.245	0.068

r: The Pearson correlation coefficient.

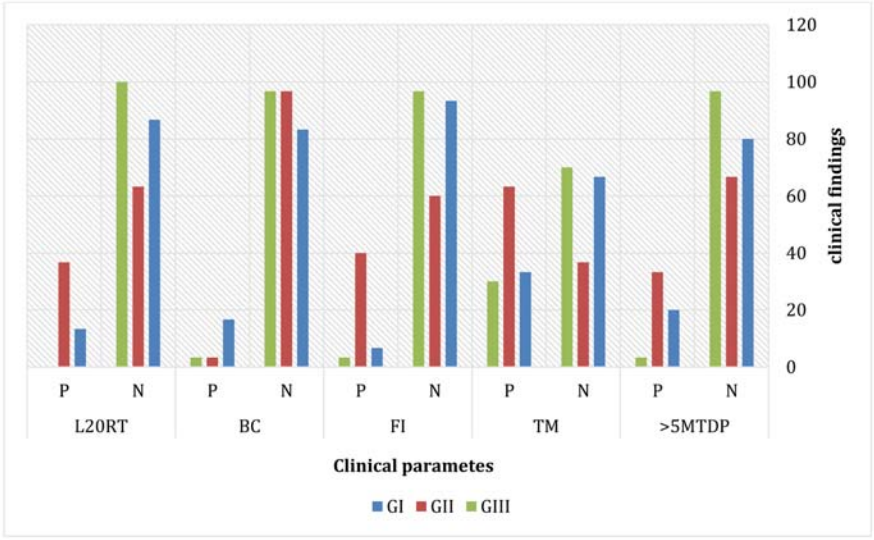


Figure 4. The clinical periodontal parameters of periodontal diseases staging complexity. G: Group, >5 MTDP: More than 5 missing teeth due perio. Diseases, TM: Tooth mobility, FI: Furcation Involvement, BC: Bite collapse, L20RT: Less than 20 remaining teeth (10 Opposing pairs), P: Positive, N: Negative.

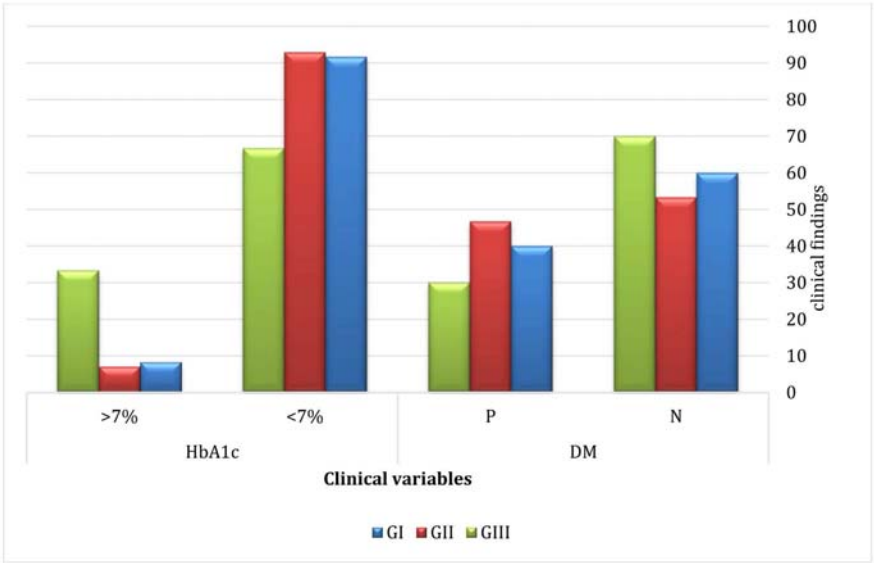


Figure 5. The participants' distribution according to some periodontitis grading modalities. G: Group, DM: Diabetes Mellitus, HbA1c: Glycated hemoglobin, DM: Diabetes Mellitus, HbA1c: Glycated hemoglobin, P: Positive, N: Negative.

The participants' ages in the present study ranged from 18 to 80 years, where the means ages of non-passive e-cigs smokers and non-smokers (Group I), e-cigs users (Group II), and passive e-cigs smokers (Group III) were 32.3 ± 14.07 years, 34.1 ± 8.84 years and 31.7 ± 5.5 years, respectively. These results confirmed the hypothesis that the mean age of e-cigs smokers is 19 years (youngers), whereas the mean age of cigarette smokers reaches 34 years [43] [44].

There is a common misapprehension that e-cigs are less impact on periodontal tissues as disagreed with the results of this study which revealed a significant

rise in the destruction of the periodontal tissues compared to those of non-smokers. The results of this study showed an increase, relating to PCR, GBI, % RBL as well as the percentage of participants with missing teeth more than five teeth due to periodontal diseases, percentage of participants affected with TM, percentage of affected participants with FI and percentage of affected participants with Less than 20 remaining teeth among the e-cigs smokers moreover an increasing relating to CAL and PPD among passive e-cigs smokers considered in this study. The PCR increase among e-cigs smokers and passive e-cigs smokers, detected in the present study, could be related to the defect in the capacity of e-cigs smokers and passive e-cigs smokers in their oral hygiene measures. In contrast, the GBI increasing among e-cigs smokers, detected in the present study, disagree with clinical proof that nicotine produces peripheral blood vessels vasoconstriction, thus decreasing gingival bleeding [45]. An increase relating in periodontitis staging and complexity parameters among e-cigs smokers and passive e-cigs smokers could be explained by the reality that nicotine acts as a participating factor to periodontal destruction by impacting the capability of fibroblasts collagen and integrin production as well as stimulation of proinflammatory cytokines production in periodontal tissues [46] [47] [48]. The results of this study confirm that those who consume tobacco are susceptible to periodontal diseases, nevertheless of the tobacco product type [6].

These clinical findings agree with other American studies that revealed a link between e-cigs smoking and more incidence of periodontal diseases and poor oral health status, which may be due to the chemicals and toxicants discharged from e-cigs [49] [50].

The clinical findings of this study also agree with other studies, which showed a potential association between passive smoking and periodontal disease [51] [52].

Concerning the control group in this study, the difference in the PCR, GBI, CAL, % RBL, and PPD were no significant differences between e-cigs users and passive e-cigs users. Whereas, the difference in the percentage of participants who were affected with more than 5 teeth missing due to periodontal diseases, TM, FI, and less than 20 remaining teeth (10 Opposing pairs) were with significant differences between e-cigs users and passive e-cigs users. This incidence raises an inquiry because e-cigs are supposed to be less damaging effects on periodontal health as a substitution method for stopping traditional smoking [53].

According to a previous study, the accurate salivary pH varied between 6.2 and 7.6, agreeing with our study results, which revealed ranges of salivary pH between 6.3 and 6.8 [54]. On the other hand, another study revealed that there were no statistically significant differences in salivary pH between e-cigs users and non-smokers, harmonious with our study results [55]. Moreover, the salivary pH values in smokers were lower than in non-smokers, according to the results of Parmar *et al.*, and Grover *et al.*, studies [56] [57]. Similar findings were recorded by our study, where the salivary pH values among e-cigs smokers were lower than non-smokers and passive e-cigs smokers without statistical signifi-

cant differences. The study of Kumar *et al.* showed that salivary pH values of tobacco smokers with periodontal diseases were lower than non-smokers with periodontal diseases, which agrees with the clinical findings of our study [58].

5. Strength and Limitations

This study adds to the previous studies, which revealed a decrease in the addiction to nicotine in traditional cigarettes with e-cigs use. Thus it is considered a method for helping all smokers who need to leave smoking. Despite several studies clarified that the main ingredients of e-cigs liquids could be possibility hurtful due to unknown impacts of these ingredients on the human body [59].

Until now, there was a shortage of studies conducted at King Khalid University on the periodontal health of e-cigs smokers and passive e-cigs smokers. Consequently, the clinical findings of this study can help clarify the harmful impacts of e-cigs smoking and passive e-cigs smoking on the periodontal tissues compared to non-smokers. Furthermore, the design of this study in the oral and periodontal health scope was to discuss the importance of changing from traditional cigarette smoking to e-cigs smoking can support the improvement of oral health and periodontal status, which reflect positively on the patient's general health.

The limitations of the present study included that the participants of this Saudi study were representative of the Aseer region only. Also, the study was cross-sectional, which did not allow us to investigate the association between the use of e-cigs and periodontal status and salivary pH values for participants who had reported a history of e-cigs smoking habit and passive e-cigs smoking regularly every day for a year or more. Moreover, the results of this study could be impacted by the mistakes of participants' selection that depended on their reports. Moreover, e-cigs smoking duration and frequency were not included in the design of the study, and as there are no criteria of measurement to assess e-cigs smoking, therefore, it is hard to compare this study's results to the results of other studies.

6. Conclusions

The e-cigs smoking habit with passive e-cigs smoking may contribute to the pathogenesis of periodontal diseases and salivary pH due to inhaled nicotine along with different flavoring agents. The present study has revealed that e-cigs smoking and passive e-cigs smoking had unwanted impacts on periodontal status. The results detected in this study will not only provide data for more research on e-cigs smoking habit and passive e-cigs smoking effects on periodontal status and salivary pH but also other types of tobacco smoking including conventional cigarette smoking and Hookah smoking effects on periodontal status and salivary pH.

There is a rise in e-cigs users' number in the world due to the wide-spread idea that e-cigs has less impact on general health as analogized to the traditional

cigarettes. Additional studies are needed to confirm the risk of e-cigs smoking habit and passive e-cigs smoking on periodontal status and salivary pH. The results of this study could help the oral health community to establish and transfer proper notices about the safety of e-cigs smoking habits and passive e-cigs smoking; and the regulation of the new tobacco products. We recommend that enough follow-up time of e-cigs smoking effects on oral and periodontal status should be included in future studies compared to traditional smoking and assess if this method is secure for smoking stopping.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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The Role of Interventional Radiology in Splenic Trauma

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Abstract

The purpose of this case report is to discuss the different treatment options available in splenic trauma patients by following the story of Mr. H. I will focus particularly on the role of splenic arterial embolisation (SAE)—an interventional radiological procedure—and how it weighs up against its surgical counterparts. In order to give a balanced view this case report includes a literature review around splenic artery embolisation. This report concludes that when managing splenic trauma, interventional radiology (IR) is a useful tool particularly when used in conjunction with surgery. The future of this field needs to allow SAE to become a stand-alone therapy. Furthermore, research needs to investigate which cohorts of patients are best suited to which intervention such that we can capitalise on the advantages of each intervention for the benefit of all.

Keywords

Interventional Radiology, Spleen, Trauma, Surgery, Laparoscopy, Embolisation

1. Introduction

The spleen is an organ often forgotten about despite its numerous physiological roles and common injury following abdominal trauma. Management of a damaged spleen is therefore very important to understand and can take the form of medical, surgical, or radiological interventions. Which is the best to use and when should we use it?

Splenic embolization was first described by Maddison in 1973 [1]. It involves selectively disrupting the arterial blood supply at the end arterioles resulting in partial splenic infarction, decreased spleen size and increased circulating platelet count [2]. The current internationally accepted indication for SAE is the pres-

ence of extravasation of contrast medium detected on CT scan [3].

Current guidelines and research focus on SAE being offered to stable patients with low grade splenic injuries as an adjunct to non-operative management (NOM) [4] [5] [6].

However, given the many benefits that this procedure offers and its great potential, it is limiting to use it only as an adjunct to NOM. In order to fully identify its strengths and weaknesses, research needs to study SAE both in isolation as well as compared to other treatment modalities. The literature review included in the following case report aims to do this.

2. What Is the Spleen and Why Is It Important?

2.1. Anatomy

The spleen is an oval-shaped lymphoid organ located in the left upper quadrant of the abdomen between the ninth and twelfth ribs. It is approximately 12 cm long, 7 cm wide and 3 - 4 cm thick, weighing 150 g. It sits inferior to the diaphragm, posterolateral to the stomach fundus, lateral to the left kidney and superior to the splenic flexure of the colon. The spleen is held in place by the splenorenal and gastrosplenic ligaments, formed by foldings of the peritoneum. Its surrounding capsule of thin grey connective tissue is thicker at the splenic hilum where arteries and nerves enter; and venous and lymphatic vessels leave.

The surrounding fibrous capsule stems many trabeculae that carry blood vessels into and out of the parenchyma. Attached to the trabeculae is a reticular fibre network providing the structural framework of the organ. The interstices of this network are filled with venous sinuses and the parenchyma—split into the lymphocyte-rich white pulp, and the red pulp [7] [8].

2.2. Function

In the red pulp, macrophages remove senescent erythrocytes and pathogens from the circulation. The inner white pulp is organised lymphoid tissue, here macrophages engulf antigens for presentation to T- and B-lymphocytes stimulating antibody-secreting plasma cell formation. Interestingly during foetal development, the spleen acts as a minor site of haematopoiesis however this function can reappear in adulthood as a compensatory mechanism in those with chronic anaemia [8] [9].

2.3. Blood Supply

Approximately 5% - 10% of the cardiac output reaches the spleen via the splenic artery, a branch of the coeliac artery. Within the spleen, the artery divides many times to supply the pulp as shown in **Figure 1**.

Whilst we know that the terminal arterial capillaries deliver blood to the splenic sinuses, the method of delivery is not completely understood. There are currently two theories of splenic arterial circulation: closed circulation and open.

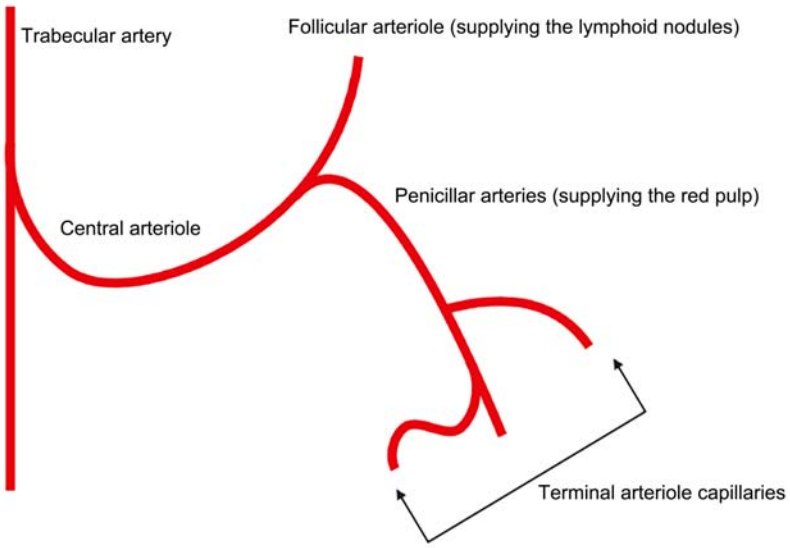

Figure 1. Example of the arterial branching tree within the spleen.

The closed circulation theory argues that the endothelial lining of the terminal arterial capillaries is continuous with that of the sinus [10]. On the other hand, the open-circulation theory states that the capillaries terminate before reaching the sinusoids, and blood drains through the red pulp into the sinuses [11]. That said, some believe that both systems co-exist – a combined open and closed circulation [12].

The splenic sinsuses are drained by small veins of the pulp that merge to form the splenic vein, a tributary of the portal vein.

3. Splenomegaly

Splenomegaly is an abnormal increase in spleen size and is the most common clinical splenic abnormality. William Osler once said "nearly all diseases of the spleen are of a secondary nature" [13]. Thus, whilst splenomegaly is often the first manifestation of disease, even in 1908 Osler was aware that numerous different pathologies manifest as splenomegaly, making it a diagnostic challenge [14].

Radiologically we can classify splenomegaly as:

Moderate—the largest dimension is between 11 - 20 cm.

Severe—the largest dimension is greater than 20 cm [15].

The pathophysiology of splenic enlargement varies with aetiology. In the case of acute infection such as endocarditis, there is increased workload of clearing antigens and producing antibodies. The spleen responds by increasing its capacity of reticuloendothelial cells to compensate splenic hyperplasia.

The spleen can also enlarge due to a vascular change. As a result of long-term liver disease and cirrhosis, portal hypertension can occur. The splenic vein drains into the hepatic portal vein however in portal hypertension this becomes congested and thus the splenic vein engorges due to the backlog [16].

As mentioned earlier, the spleen may also re-assume a haematopoietic role in adults with chronic anaemia. This extramedullary haematopoiesis is often exhibited in myeloproliferative disorders and causes an increase in spleen size to accommodate the added function.

Finally, as with any organ in the body, the spleen is a potential site for infiltration. This may either be invasion of foreign cells such as metastases, or neoplastic changes within resident immune cells as seen in lymphoma [16] [17].

Complications

The most feared complication of splenomegaly is splenic rupture, usually caused by blunt abdominal trauma. In very thin individuals, the degree of trauma can be minor and may even be unnoticed.

The reason splenic rupture is so dangerous is because life-threatening intraperitoneal haemorrhage may follow. If there is associated hypersplenism also present, haemorrhage is even more dangerous due to thrombocytopaenia slowing clot formation [16].

4. Common Splenic Interventions

4.1. Splenectomy

If splenic rupture is severe to the extent that the spleen has been avulsed from its vascular pedicle, an emergency splenectomy would be necessary.

Splenectomy refers to the surgical procedure in which the spleen is partially or totally removed, this can be performed laparoscopically or open. Elective splenectomies favour a laparoscopic approach provided the spleen is not too big whilst the open technique is usually reserved for emergency trauma, or spleens which are massively enlarged [18] [19].

4.2. Other

For less severe damage, modern thrombostatic surgical or radiological techniques can sometimes permit partial preservation such that the entire spleen need not be removed.

5. Case Clinical History and Examination

The following section will discuss the case of Mr. H, a 54-year-old gentleman whose story forms the centrepiece of this report and allows a case-based view on splenic pathology and management.

Between April and June 2020, Mr. H noticed his urine had become more "sticky". On presenting to his GP, a diagnosis of diabetes mellitus was confirmed by HbA1c. A full blood count performed at the same time showed a profound iron deficiency anaemia and on further questioning, it became apparent that the patient had also experienced weight loss and a few episodes of night sweats. As a result, the patient was referred to a haematology lymphoid clinic where a CT scan showed a moderately enlarged spleen and some enlarged abdominal lymph

nodes. CT-guided biopsy confirmed these changes to be due to a low-grade B-cell non-Hodgkin lymphoma. Due to being low grade, the initial management plan was to watch and wait.

By the end of January 2021 however, an MDT discussion decided that because the patient's symptoms were worsening it would be suitable to commence treatment with R-CVP (rituximab, cyclophosphamide, vincristine, and prednisolone).

In April, Mr. H suffered a fall out of bed landing on his front sustaining a left-sided chest and abdominal injury. His A&E clerking notes reported that he was pale and shivering with confusion, hypotension and a tender and distended LUQ abdomen. A CT abdomen showed a splenic laceration with active bleeding and a large volume haemoperitoneum. His notes showed that a prior abdominal ultrasound revealed splenomegaly of 17.6 cm. The patient was given a blood transfusion and referred to the surgical emergency unit where a joint decision was made for Mr. H to be managed with SAE under IR.

During the procedure, a focal active bleed was found at the lower splenic pole, supplied by multiple splenic branches. These were selectively cannulated with a co-axial microcatheter and embolised with multiple micro-coils. No further bleeds or abnormalities were seen and the splenic artery supply to the majority of the spleen was preserved. Mr. H suffered no post-procedure complications and on examination his abdomen was distended but soft with some tenderness on palpation but no signs of bleeding.

6. What SAE Is and Involves

Patients who injure their spleen can broadly be categorised into those who are unstable, and those who are stable. Unstable patients generally undergo laparotomy and splenectomy due to the emergent nature of the injury and the increased risk of mortality [20]. Stable patients with lower grade injuries are treated more conservatively with non-operative management (NOM), with or without SAE added as an adjunct to increase the success rate of NOM [20] [21] [22].

SAE can be categorised into two main types – proximal and distal. Proximal SAE (PSAE) acts to decreases systolic arterial perfusion pressure whilst simultaneously promoting haemostasis and healing due to maintenance of blood flow via collateral pathways. Distal SAE (DSAE) is more beneficial in cases of focal injury. Given that blunt splenic trauma more commonly causes a multifocal injury, it is unsurprising that PSAE is the more commonly carried out procedure [23].

Figure 2 shows the major blood vessels supplying the spleen. The splenic artery is one of three branches of the coeliac trunk. Its first large branch is typically the dorsal pancreatic artery which bifurcates into left and right branches; the left branch continuing as the transverse pancreatic artery. The second large branch of the splenic artery is the greater pancreatic artery.

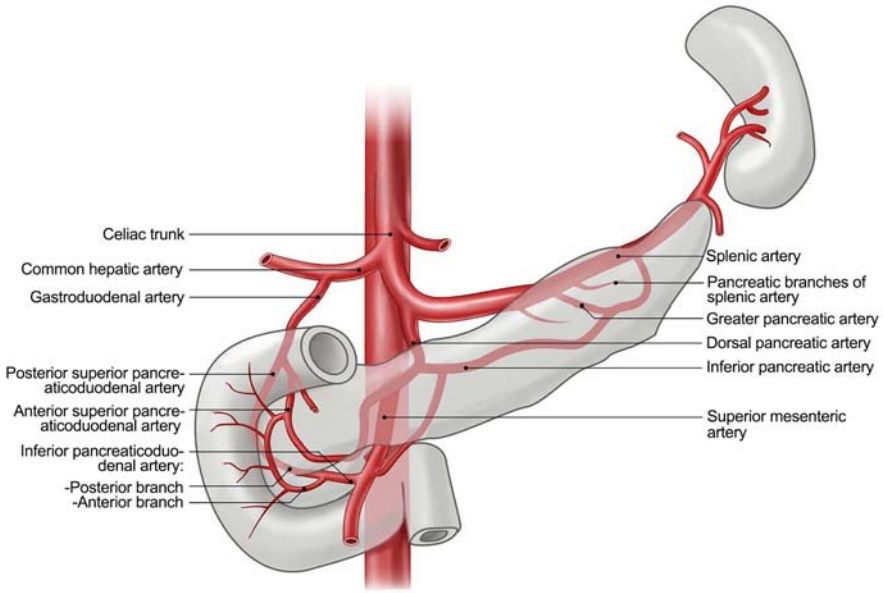

Figure 2. Major blood supply to spleen and surrounding structures Ref amboss.com.

Embolisation Technique

SAE is typically performed via a trans-femoral approach. The coeliac trunk is engaged using a 5 Fr reverse curve catheter. Coeliac angiogram is then performed, with images evaluating splenic artery patency, tortuosity, size, and pattern of injury. The other branches of the coeliac trunk are also evaluated as these will be important in supplying collateral perfusion to the spleen following PSAE.

To perform DSAE, a microcatheter and microwire are advanced to the site of the vessel injury and embolisation occurs with particles, glue (such as N-butyl cyanoacrylate), gel-foam and/or coils. For PSAE, vascular plugs and/or coils can be used between the dorsal pancreatic artery and great pancreatic artery. Alternatively, PSAE can be performed following DSAE, the rationale for this combined approach being that some vascular injuries may not be visible on initial angiogram and may lead to delayed bleed once vasospasm subsides [24] [25].

7. Literature around IR Embolisation

As mentioned earlier, other interventions for managing splenic pathology do exist, so why do we perform SAE?

7.1. Advantages of SAE

SAE has been shown to have numerous benefits in a wide number of settings. Vittorio et al showed that prophylactic SAE significantly improved platelet count in 80.8% of paediatric patients with thrombocytopaenia. Furthermore, children with prior oesophageal varices showed improvement after SAE with only 34.6% requiring further endoscopic therapy. The group concluded that prophylactic SAE is a safe and effective alternative in the management of different groups of paediatric patients [2].

SAE also preserves functional spleen mass (and therefore immunological function) while avoiding post procedure acceleration of underlying liver disease [23]. This is supported by studies from Kis *et al.* who used IgM memory B cell levels as a quantitative measure of immunological function to show that long-term immune function is preserved in cancer patients post-SAE [23] [24]. A few years later, the same group showed that SAE improved platelet counts in cancer patients despite different aetiologies of splenomegaly [23]. Other groups have also confirmed the absence of Howell-Jolly bodies in patients post SAE thus confirming preserved splenic phagocytic function.

Splenic insufficiency due to splenectomy has the major clinical manifestation of an increased susceptibility to sepsis caused by encapsulated bacteria such as pneumococci, meningococci, and *Haemophilus influenzae.* This is due to the decrease in phagocytic capacity and antibody production. All asplenic individuals therefore must be vaccinated against these agents to reduce septic risk. Since SAE does not result in asplenia, these problems are completely avoided reducing future hospitalisations and deaths due to septic complications.

The procedure itself is much less invasive compared to surgical management. This has benefits on two fronts, first it gives SAE the versatility of being performed in both emergent and elective settings. Second it allows for faster recovery, reduced hospitalisation time and radiation dose from repeated imaging and ultimately reduced cost [25].

On the topic of cost, studies by Yip et al have shown that splenic embolisation is a low-cost procedure when compared against previously modelled data from overseas studies. The use of ICU for monitoring after a procedure significantly increases its cost, hence surgical interventions are more likely to be more expensive [25].

Parihar et al showed that patients who underwent SAE followed by NOM had a significant increase in haemoglobin, haematocrit levels and systolic blood pressure compared to those who were only managed with NOM. The mean length of hospital stay was lower in the SAE group and the need for secondary splenectomy was significantly lower as well. The authors suggested that this difference may be due to better haemostasis, facilitation of clot formation, and earlier healing achieved by SAE. On the other hand, patients managed with NOM may have continuous ongoing bleeding from the injured spleen leading to delayed and slowed healing [21].

Overall, there are clearly numerous benefits of SAE. It is for these many reasons that groups such as Clements et al argue that SAE should become a stand-alone treatment option for splenic trauma as opposed to an adjunct to NOM [26]. This also adds to the bigger picture of the rising predominance of IR as a field and how this fast-growing specialty will soon be performing a lot of unique procedures that will change the world of surgery.

7.2. Disadvantages of SAE

It would be blind to assume that SAE is a technique without faults. The follow-

ing section will discuss some of the negative aspects of SAE.

As with any procedure, SAE does have risks and complications attached to it. Many post-op patients, suffer from transient abdominal pain, distention and fever secondary to perisplenic abscesses [27].

More severe complications include splenic rupture and infarction; pancreatic infarction; severe hepatic insufficiency; and cardiac insufficiency all of which can cause death.

Duchesne *et al.* reported a higher incidence of acute respiratory distress syndrome (ARDS) after SAE, something that is concerned about now more than ever given the association of ARDS with Covid-19 related deaths [26]. A theoretical disadvantage of SAE is re-bleeding distal to the coils/plugs. This would necessitate re-intervening endovascularly through collaterals to perform subsequent embolisation, thus adding on the risks of further interventions [27].

Furthermore, it could be argued that another disadvantage of SAE is the exposure to ionising radiation, particularly to the operators. However, to counter this, a recent study by Omer *et al.* showed no significant short-term danger to the health of personnel by placing TLD dosimeters at different body areas [22].

All these aside however, the worst fact of all is that the potential long-term complications resulting from SAE are unknown in the trauma population and what we do not know, we cannot protect our patients against [28].

8. Is IR the Saviour of the Spleen?

How does IR SAE compare against its surgical counterparts? 30 years ago, the world of surgery was celebrating the innovation of laparoscopic techniques, has IR made those redundant?

Some of the benefits of SAE over surgery have already been mentioned such as the reduced invasiveness of IR as well as the functional splenic mass that is left over. Both allow for faster recovery and fewer long-term complications associated with asplenia [14]-[19]. For such reasons, many trauma centres are now performing more embolisation procedures than splenectomies [21] [25].

However, to say that SAE is better than a surgical approach is too simplistic.

Before the rise of IR, splenectomy was commonly performed in cases of splenomegaly increasingly laparoscopically. The advantages of such minimally invasive surgery were dramatic on their impact on postoperative pain, morbidity, and length of hospitalisation. The views that modern laparoscopes allow, give clarity in viewing anatomical structures allowing careful navigation around the many splenic vessels, such that they can be safely and appropriately ligated and transected [13].

Where laparoscopic splenectomy (LS) is a weaker intervention are in cases of massive splenomegaly where open splenectomy (OS) is a safer alternative. In fact, studies have shown that the most dangerous operations were those where initial LS had to be converted to OS due to the large size of the spleen [27]. Thus, spleen size is a very important factor when deciding which intervention will be the most beneficial [12] [28].

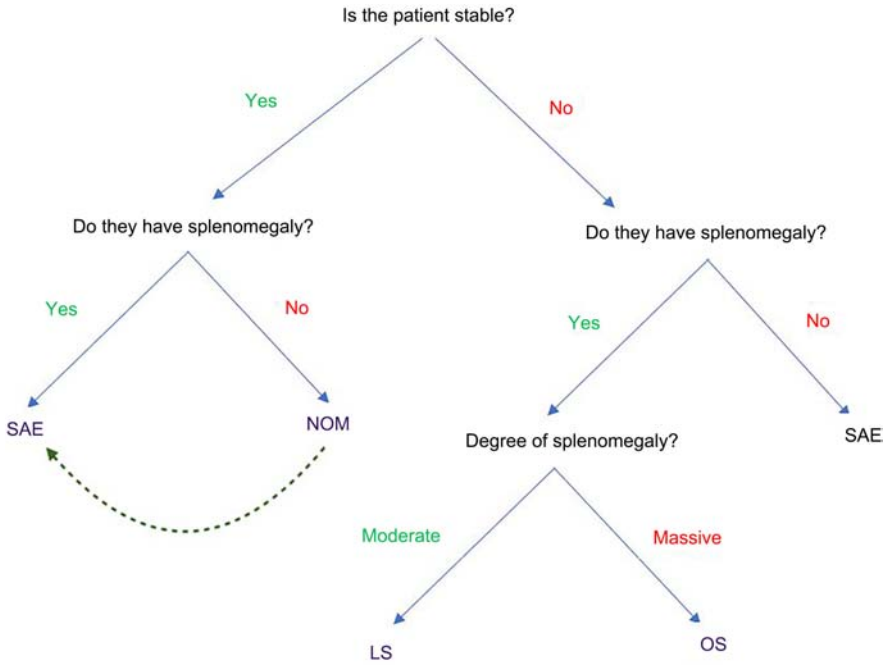

Figure 3. Flowchart suggesting a method of dividing the different managements of splenic laceration dependent on patient stability and degree of splenomegaly. * Massive splenomegaly represents a spleen exceeding 1000 g of weight and 20 cm in greatest dimension [30]. Alternatively, one can use a radiological criterion [9]. SAE: splenic artery embolisation; NOM: non-operative management; LS: laparoscopic splenectomy; OS: open splenectomy.

It is also important not to forget the importance of NOM and the large shift towards NOM in the past decade. The benefits include there being even less risk of infection with encapsulated bacteria compared to SAE. Furthermore, it can be helpful in cases where a patient may not be fit enough for invasive intervention.

The disadvantages of NOM include a risk of delayed splenic rupture, the possibility of re-bleeding as well as complications of embolisation. A more niche point is that unlike with surgical intervention, with NOM there is no intra-operative view that can be obtained of other visceral organs allowing less of an assessment of overall disease progress [15].

9. Conclusions

A study in 2016 showed that just under 200,000 people die each year from injury, 1 person every 3 minutes [29] [30]. The prevalence of intra-abdominal injury amongst emergency department patients is around 15%, and the spleen is the most injured organ in blunt abdominal trauma [30] [31].

This case report has used the example of Mr. H to discuss the different managements of splenic laceration. We have seen that SAE is becoming increasingly popular due to its reduced invasiveness, minimal splenic disruption, and faster recovery times with fewer post-op complications. That said, its surgical counterparts are still advantageous depending on both the degree of splenomegaly, and the stability of the patient.

The future of this field therefore needs to allow SAE to become its own stand-alone therapy rather than just being an adjunct to NOM. Furthermore, research needs to investigate which cohorts of patients are best suited to which intervention such that we can capitalise on the advantages of each intervention for the benefit of all. **Figure 3** shows one example of how we may divide up these interventions, it could be altered to fit different criteria such as AAST grade of injury.

Hopefully, this report has made it clear that regarding management of the spleen, IR is a rising star but currently I do not believe that it can replace surgical intervention altogether.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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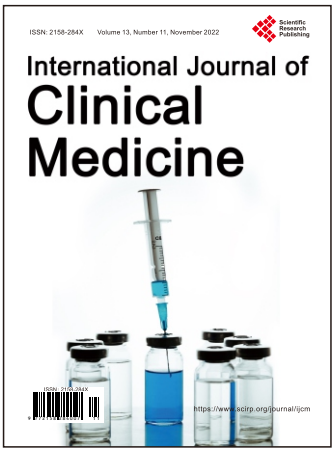

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- Clinical Neuroscience
- Clinical Nursing
- Clinical Nutrition
- Clinical Obstetrics and Gynaecology
- Clinical Oncology and Cancer Research
- Clinical Ophthalmology
- Clinical Oral Implants Research
- Clinical Oral Investigations
- Clinical Orthopaedics and Related Research
- Clinical Otolaryngology
- Clinical Pathology
- Clinical Pediatric Emergency Medicine
- Clinical Periodontology
- Clinical Pharmacology & Toxicology
- Clinical Pharmacy and Therapeutics
- Clinical Physiology and Functional Imaging
- Clinical Practice and Epidemiology in Mental Health
- Clinical Psychology and Psychotherapy
- Clinical Psychology in Medical Settings
- Clinical Radiology
- Clinical Rehabilitation
- Clinical Research and Regulatory Affairs
- Clinical Research in Cardiology
- Clinical Respiratory
- Clinical Rheumatology
- Clinical Simulation in Nursing
- Clinical Sleep Medicine
- Clinical Techniques in Small Animal Practice
- Clinical Therapeutics
- Clinical Toxicology
- Clinical Transplantation
- Clinical Trials
- Clinical Ultrasound
- Clinical Virology
- Complementary Therapies in Clinical Practice
- Consulting and Clinical Psychology
- Contemporary Clinical Trials
- Controlled Clinical Trials
- Diabetes Research and Clinical Practice
- Evaluation in Clinical Practice
- Fundamental & Clinical Pharmacology
- Hereditary Cancer in Clinical Practice
- Human Psychopharmacology: Clinical and Experimental
- Innovations in Clinical Neuroscience
- Laboratory and Clinical Medicine
- Neurophysiologie Clinique/Clinical Neurophysiology
- Nutrition in Clinical Practice
- Pacing and Clinical Electrophysiology
- Psychiatry in Clinical Practice
- Therapeutics and Clinical Risk Management
- Veterinary Clinical Pathology

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