Methods of Blood Loss Quantification in Major Abdominal Surgery: A Narrative Review

Ján Zajak[1,2], Jiří Páral[2], Miroslav Sirový[1,2], Šárka Odložilová[1,2], Kateřina Vinklerová[1,2], Michal Balík[3], Filip Čečka[2,*]

ABSTRACT

Blood loss in major abdominal surgery is an essential parameter in the evaluation of strategies aimed at reducing perioperative bleeding. It is also an important parameter of quality of the surgical procedure, along with postoperative morbidity and mortality, radicality of the surgical resection, etc. However, blood loss quantification remains unreliable and inaccurate.
The methods used to measure blood loss can be categorized as visual estimation, gravimetric method, direct measurement, spectrophotometry, calculation methods, colorimetric analysis, and miscellaneous. The aim of this work is to review up-to-date knowledge about the various methods of blood loss quantification and then to introduce study, which should compare more methods of blood loss quantification in a real surgical setting.

AUTHOR AFFILIATIONS

[1] Department of Military Surgery, University of Defence, Military Faculty of Medicine, Hradec Králové, Czech Republic
[2] Department of Surgery, University Hospital and Charles University, Faculty of Medicine, Hradec Králové, Czech Republic
[3] Department of Urology, University Hospital and Charles University, Faculty of Medicine, Hradec Králové, Czech Republic
* Corresponding author: Department of Surgery, University Hospital and Charles University, Faculty of Medicine, Sokolská 581, 500 05 Hradec Králové, Czech Republic; e-mail: filip.cecka@fnhk.cz

INTRODUCTION

Blood loss during major abdominal surgery is an essential parameter in the evaluation of strategies aimed at reducing perioperative bleeding such as pharmacological interventions, anaesthetic management, and surgical techniques. Blood loss estimate is an important parameter of quality of the surgical procedure, along with postoperative morbidity and mortality, radicality of the surgical resection, number of retrieved lymph nodes, duration of the surgical procedure, or some other parameters (e.g. postoperative pancreatic fistula in case of pancreatic resections, biliary leak in case of liver resection, or anastomotic leak in case of biliary reconstruction) (1–4).

Quantified blood loss plays a key role in blood transfusion decisions, along with other information such as haemoglobin values and individual transfusion triggers. Negative impact of intraoperative blood loss on outcomes has been well characterized in many studies. Inappropriate transfusion of blood products is associated with risks and influences patient's outcome (5). Lower blood loss contributes to better perioperative outcomes (6).

It is important and very well-known fact that perioperative transfusions affect long-term outcome in patients undergoing liver resection for primary liver tumours, metastatic colorectal cancer and also in patients undergoing pancreatic resection (7, 8). Blood transfusion produces host immunosuppression and has been postulated to result in adverse outcome for patients undergoing surgical resection of malignancies. Blood transfusion is associated with adverse outcome and this effect is dose-related. Even patients receiving only one or two units have a more adverse outcome. Blood conservation methods should be used to avoid transfusion, especially in patents currently requiring limited amounts of transfused blood products (7, 8).

However, blood loss quantification remains unreliable and inaccurate (9–13). It is noteworthy that loss of lower blood volumes is estimated more correctly than loss of higher blood volumes. However, large blood loss is life-threatening and therefore more relevant in transfusion decisions. The methods used to measure blood loss can be categorized as visual estimation, gravimetric method, direct measurement, spectrophotometry, calculation methods, colorimetric analysis, and miscellaneous (5, 14). The aim of this work is to review up-to-date knowledge about the various methods of blood loss quantification and then to introduce study, which should compare more methods of blood loss quantification in a real surgical setting.

VARIOUS METHODS OF BLOOD LOSS EVALUATION

There are several methods of blood loss evaluation in surgical procedures. They range from simple visual estimate, through more precise methods, e.g. gravimetric method, direct measurement method, calculation method to spectrophotometric method, which is considered as the most precise one.

Visual estimation of blood loss is still the standard method of choice in many cases. It is the simplest method, on the other hand, it is also the most inaccurate (15). Apart from measuring the volume of the suctioned blood in the suction canisters, a visual estimate of blood shed on the floor, spread in the surgeons' gowns and gloves and hidden in drapes and sponges must be done. A broad deviation of the visual estimates and little coincidence with the actual values has been found (15). Over- and underestimations by 2 or even 3-fold are rather common; underestimations are more frequent. A significant trend to overestimate diluted blood was found. Even though these certain sites were known to exhibit diluted blood, e.g. suction canisters. On the other hand, laparotomy pads and sponges fully saturated with blood are grossly underestimated. Age, gender and length professional experience of the physicians does not influence the magnitude of estimation errors. Only the professional groups' estimates differ: anaesthetists tend to overestimate, on the other hand orthopaedic or general surgeons tend to underestimate the blood loss. Irrigation fluids, lymph, bile, serum, ascites, urine, and other fluids often combine with lost blood, but do not alter its appearance to an extent that is typically appreciable visually, which can affect estimated blood loss (16). Visual estimation of operative blood loss is unreliable and inaccurate. No provider specialty, level of experience, or self-assessment of ability is associated with improved estimation (17). Very often, visual estimate of blood loss relies on a discussion between a surgeon and an anaesthesiologist until a consensus is reached (18).

The **gravimetric method** was first described by Wangensteen (19). It is based on weighing surgical sponges before and after surgical use. Estimated blood loss is determined by assessing the weight difference before and after use, with every gram of weight equivocal to 1 mL of blood loss (18). For minor procedures in which major blood loss is not expected, accurate measurement is trivial. For procedures in which major blood loss is expected, such as during orthopaedic surgery, allogeneic blood transfusion is often the mainstay for intraoperative and postoperative hemodynamic management, making accurate determination of blood loss a necessity. The gravimetric method is easy but neither precise nor accurate (20), especially with increased dilution by rinsing fluid (21, 22).

Direct measurement of blood loss is also a simple and long-established method that is mainly used in the field of obstetrics (5). A calibrated collection bag with a scale is designed especially for vaginal deliveries. Current blood loss can be immediately read from the scale (23, 24). Blood loss measurement in vaginal deliveries is especially important because studies of maternal deaths show that most deaths due to postpartum haemorrhage involve delayed and substandard care in the diagnosis and management of blood loss (23).

Delay in the diagnosis and treatment of postpartum haemorrhage may result from an underestimation of blood loss at delivery. Assessment of postpartum blood loss, particularly after vaginal birth, is recognised as difficult. Many studies found that visual estimates of peripartum blood loss are often inaccurate, showing an overestimation

of blood loss at low volumes and an underestimation at larger volumes, the magnitude of underestimation typically increasing with the volume of haemorrhage (25).

When bleeding is excessive but before haemorrhage has become catastrophic, appropriate management will take place without delay, so reducing the incidence of severe postpartum haemorrhage. Study results show significant deviations from real blood loss (23). Lack of identification of women with excessive postpartum bleeding is a problem, potentially leading to higher levels of medical intervention if the bleeding progresses to severe haemorrhage.

Calculation Method: Various mathematical approaches can be used to calculate blood loss in current clinical practice. There are several mathematical formulas and they have been modified over time: Nadler, Liu, Mercuriali, Bourke, Ward, Gross, Lisander, Meunier, Camarasa, Lopez-Picado. All calculation formulas require an estimation of the total blood volume of the patient. The formulas take into account height, weight, body surface area and gender of the patient (26, 27). Perioperative red blood cell loss (RBCL) is calculated by adding the difference in circulating red blood cells from before to after surgery (28–31). The formulas take into consideration volume of blood transfusion, they differentiate between autologous and homologous blood. All blood loss estimation formulas showed a significant tendency to overestimate blood loss (5, 9, 32).

Spectrophotometry is the most precise, but also the most expensive and complex to use. It is considered to be a benchmark for measurement of the blood loss (18). Haemoglobin mass loss is assessed in the lost blood using the spectrophotometric method.

With this method, intraoperative samples extracted from surgical sponges and suction canisters are measured postoperatively with absorption spectrometry, enabling direct haemoglobin (Hgb) measurement within the samples. Spectrophotometric measuring of haemoglobincyanide is the reference method for haemoglobinometry in human blood recommended by the International Council for Standardization in Haematology since 1967 (ICSH) (33). However, the main drawback of this method is a lack of practical and accurate real-time intraoperative EBL assessment. The blood los sis actually calculated after the end of the surgical procedure (18).

Colorimetric blood loss estimation – a smartphone application (Triton™) developed by Gauss Surgical Inc. is able to calculate blood loss by taking photographs of used surgical gauze and canisters. The colorimetric technique analyses photographic and geometric information from relevant areas, with the aim of automatically filtering out the effects of non-blood components mixed in each sponge and canister and calculating the Hb mass present in the gauze or canister from the image. By entering the preoperative Hb-level, the blood loss can then be calculated (5). This method has been found to be accurate across many sponge types and lighting conditions (22) as well as to be an accurate determinant of blood loss assessment in adult patients (21). High degrees of correlation with the reference blood volumes were found in several studies, however only with limited number of patients (21, 22, 34–37). Large studies with more patients are needed to confirm these results.

DISCUSSION

Even though, there are many methods of blood loss quantification or estimation, no study yet compared more methods to assess the deviations from the spectrophotometry as the most accurate method.

We decided to conduct a clinical trial in order to compare several methods of blood loss quantification or estimation in real surgical settings. The primary aim of the trial is to compare several methods of blood loss quantification, e.g. visual estimation by a surgeon (sEBL) and an anaesthesiologist (aEBL), gravimetric method (vGBL), calculation method (vCBL), and spectrophotometry in real surgical settings. We hypothesized that visual estimation, gravimetric measurement, and calculation method will significantly differ from measured haemoglobin loss by spectrophotometry.

All adult patients who are scheduled for elective liver or pancreas surgery in our department are assessed as participants of the trial. Signed informed consent must be provided. Operating surgeon must have experience with at least 200 cases. Patients with coagulation disorder or unable or unwilling to participate are excluded.

Patients are assessed for eligibility in the study, and their anthropometric data (height, weight) and clinically relevant data is recorded prior to the surgery. Venous blood samples for blood count (including haematocrit and haemoglobin concentrations) are drawn before incision, at one hour after closure, and at 24 and48 hours after surgery. All samples are analysed at the central laboratory using an automated haematology analyser XN-10 (Sysmex, Kobe, Japan).

The suction canister is heparinized before surgery (10,000 IU of heparin in 100 ml saline solution) to prevent clotting. The total volume contained in the canister is measured after the end of the surgical procedure by a system capable of determining differences up to ±10 mL and weighted by a Kern, PCB 6000-0 with an accuracy of ±1 g (Balingen, Germany). The sample from the canister is analysed for haemoglobin concentrations by spectroscopy using the XN-10 (Sysmex, Kobe, Japan), and cell count in "body fluid" mode, which is more sensitive to lower cell counts in fluids.

The volume of irrigation fluids used during surgical procedure is carefully recorded as well as infusions, injections and transfusion volume. If necessary, vasoactive agents are titrated to obtain a mean blood pressure of >65 mmHg during procedure. All laparotomy pads are weighted and counted before and after surgery. At the end of the operation, an estimated blood loss is obtained from the anaesthesiologist and surgeon. Postoperative complications are graded based on severity according to the Clavien-Dindo definition (38).

The primary outcome of the trail is to compare several methods of blood loss quantification (visual estimation by surgeon and anaesthesiologist, gravimetric method, calculation method, and spectrophotometry) in real surgical settings.

The anaesthesiologist and surgeon's estimate of blood loss is based on a visual assessment of blood loss in the

suction canister and surgical pads after subtracting the volume of added fluids, which both know.

The suction canister and surgical pads are weighed before and after the surgical procedure. Estimated blood loss is determined by assessing the weight difference after subtracting weight of added fluids. Every gram of weight difference equivocal to 1 mL of blood loss.

For calculation method, López-Picado's formula (32) is used to estimate blood loss based on anthropometric and haematological parameters:

$$vCBL = \frac{[EBV \times (Hct_i - Hct_f) + transfused\ RBC\ volume]}{Hct_{mean}}$$

where Hct_i (initial haematocrit) is the patient's preoperative haematocrit, Hct_f (final haematocrit) is the patient's postoperative haematocrit. Postoperative time point of the final haematocrit is not specified in the original formula, therefore in accordance with another studies (1). Hct_f in this trail is determined 48 hours after surgery or when haematocrit reached the nadir level after operation. The transfused RBC volume is calculated as follows: 1 Unit packed homologous blood = 450 mL × haematocrit of the transfused blood; 1 Unit packed autologous blood = 450 mL × haematocrit in the pre-surgical anaesthesia consultation. Hct_{mean} is the mean haematocrit (between Hct_i and Hct_f). EBV is the estimated blood volume determined using the ICSH formula (27):

a) Female:
   EBV (mL) = Plasma volume (mL) + red cell volume (mL) = [weight (kg)$^{0.425}$ × height (cm)$^{0.725}$] × 0.007184 × 2.217 + age (years) × 1.06
b) Male:
   EBV (mL) = Plasma volume (mL) + red cell volume (mL) = [weight (kg)$^{0.425}$ × height (cm)$^{0.725}$] × 0.007184 × 3.064 – 825

For spectrophotometry as the most accurate method, haemoglobin mass loss for each case is calculated using the spectrophotometric measured haemoglobin concentration from the suction canister. This value is multiplied by the total volume of the suction canisters and the calculated fluid volume from surgical pads.

To obtain total lost haemoglobin mass loss:

hbMBL = hemoglobin concentration from canister × (suction canister volume + fluid volume from surgical pads)

where fluid volume from surgical pads is calculated as:

$$\frac{fluid\ volume\ from}{surgical\ pads} = \frac{(suction\ canister\ volume) \times (weight\ difference\ of\ surgical\ pads\ before\ and\ after\ use)}{weight\ of\ suction\ canister\ volume}$$

where vMBL is measured blood loss in volume units (mL).

The blood loss is calculated using measured hemoglobin mass loss (hbMBL) and patient's average pre- and postoperative hemoglobin, the vMBL is obtained:

$$vMBL = \frac{hbMBL\ (measured\ hemoglobin\ mass\ loss\ in\ g)}{mean\ (pre\ and\ postoperative)\ hemoglobin\ (in\ g/dL)}$$

The sample size calculation is based on the data from a previous study (16). According to this study power calculations revealed that a sample size of 35 pairs would be needed to detect a 2-fold difference between two methods with 83 percent power to detect the mean difference of 100 mL between these two methods. With an expected dropout rate over 20%, we plan to enrol 45 patients into the study. Patients undergoing elective liver or pancreas surgery will be recruited to reach target sample size.

In conclusion, most surgical departments use the surgeon and anaesthesiologists' visual estimations to determine blood loss during surgery. Such an estimate is, however, often inaccurate. There is no gold standard for determining blood loss in the course of surgical procedures. Determining blood loss accurately in real conditions is a difficult task for many reasons: different suctioning techniques, different use of surgical drapes (soaking part of the drapes in saline before use), different habits of instrumented nurses in the management of flushing fluid, different degrees of admixture of lymphatic fluid, bile, and ascites in the suctioned fluid throughout the course of procedures.

In order to make the measurement of blood loss as accurate as possible, it is necessary to develop a measurement methodology in real conditions that considers the above-mentioned problems.

ABBREVIATIONS

aEBL   estimated blood loss by anesthesiologist in volume units (mL)
EBV   estimated blood volume
hbMBL   measured hemoglobin mass loss in mass units (g)
Hct_i initial hematocrit, is the patient's preoperative hematocrit
Hct_f final hematocrit
Hct_{mean} mean hematocrit (between Hct_i and Hct_f)
RBC   red blood cell
sEBL   estimated blood loss by surgeon in volume units (mL)
vCBL   calculated blood loos in volume units (mL)
vGBL   gravimetric blood loss in volume units (mL)
vMBL   measured blood loss in volume units (mL)

FUNDING

COMPETING INTERESTS

The authors declare that they have no competing interests.

REFERENCES

1. Perri G, Marchegiani G, Reich F, et al. Intraoperative Blood Loss Estimation in Hepato-pancreato-biliary Surgery- Relevant, Not Reported, Not Standardized: Results from a Systematic Review and a Worldwide Snapshot Survey. Ann Surg 2023; 277: e849–e855.
2. Jarnagin WR, Gonen M, Fong Y, et al. Improvement in perioperative outcome after hepatic resection: analysis of 1,803 consecutive cases over the past decade. Ann Surg 2002; 236: 397–406.
3. Gouma DJ, van Geenen RC, van Gulik TM, et al. Rates of complications and death after pancreaticoduodenectomy: risk factors and the impact of hospital volume. Ann Surg 2000; 232: 786–95.
4. Ball CG, Pitt HA, Kilbane ME, et al. Peri-operative blood transfusion and operative time are quality indicators for pancreatoduodenectomy. HPB 2010; 12: 465–71.
5. Gerdessen L, Meybohm P, Choorapoikayil S, et al. Comparison of Common Perioperative Blood Loss Estimation Techniques: A Systematic Review and Meta-analysis. J Clin Monit Comput 2021; 35: 245–58.
6. Seykora TF, Ecker BL, McMillan MT, et al. The beneficial effects of minimazing blood loss in pancreatoduodenectomy. Ann Surg 2019; 270: 147–57.
7. Kooby DA, Stockman J, Ben-Porat L, et al. Influence of Transfusions on Perioperative and Long-Term Outcome in Patients Following Hepatic Resection for Colorectal Metastases. Ann Surg 2003; 237: 860–70.
8. Panagiotakis E, Selzer T, Böhm G, et al. Preoperative hemoglobin levels, extended resections and the body mass index influence survival after pancreaticoduodenectomy. Langenbecks Arch Surg 2023; 408: 124.
9. Jaramillo S, Montane-Muntane M, Gambus PL, Capitan D, Navarro-Ripoll R, Blasi A. Perioperative blood loss: estimation of blood volume loss or haemoglobin mass loss? Blood Transfus 2020; 18: 20–9.
10. Franchini M, Marano G, Veropalumbo E, et al. Patient Blood management: a revolutionary approach to transfusion medicine. Blood Transfus 2019; 17: 191–5.
11. Clevenger B, Mallett SV, Klein AA, et al. Patient Blood Management to Reduce Surgical Risk. Br J Surg 2015; 102: 1325–37.
12. Flordal PA. Measurement of blood loss in clinical studies. Eur J Anaesthesiol 1997; 14: 35–7.
13. Goodnough LT, Panigrahi AK. Estimating Blood Loss. Anesth Analg 2017; 125: 13–4.
14. Schorn MN. Measurement of Blood Loss: Review of the Literature. J Midwifery Womens Health 2010; 55: 20–7.
15. Meiser A, Casagranda O, Skipka G, et al. Quantification of Blood Loss. How precise is visual estimation and what does its accuracy depend on? Anaesthesist 2001; 50: 13–20.
16. Thomas S, Ghee L, Sill AM, Patel ST, Kowdley GC, Cunningham SC. Measured *versus* estimated blood loss: interim analysis of a prospective quality improvement study. Am Surg 2020; 86: 228–31.
17. Rothermel LD, Lipman JM. Estimation of blood loss is inaccurate and unreliable. Surgery 2016; 160: 946–53.
18. Nowicki PD, Ndika A, Kemppainen J, et al. Measurement of intraoperative blood loss in pediatric orthopaedic patients: evaluation of a new method. J Am Acad Orthop Surg Glob Res Rev 2018; 2: e014.
19. Wangensteen OH: The controlled administration of fluid to surgical patients. Minn Med 1942; 25: 783.
20. Johar RS, Smith RP. Assessing gravimetric estimation of intraoperative blood loss. J Gynecol Surg 1993; 9: 151–4.
21. Holmes AA, Konig G, Ting V, et al. Clinical evaluation of a novel system for monitoring surgical hemoglobin loss. Anesth Analg 2014; 119: 588–94.
22. Konig G, Waters JH, Javidroozi M, et al. Real-time evaluation of an image analysis system for monitoring surgical hemoglobin loss. J Clin Monit Comput 2018; 32: 303–10.
23. Zhang WH, Deneux-Tharaux C, Brocklehurst P, Juszczak E, Joslin M, Alexander S; EUPHRATES Group. Effect of a collector bag for measurement of postpartum blood loss after vaginal delivery: cluster randomised trial in 13 European Countries. BMJ 2010; 340: c293.
24. Legendre G, Richard M, Brun S, Chancerel M, Matuszewski S, Sentilhes L. Evaluation by obstetric care providers of simulated postpartum blood loss using a collector bag: a French prospective study. J Matern Fetal Neonatal Med 2016; 29: 3575–81.
25. Stafford I, Dildy GA, Clark SL, Belfort MA. Visually estimated and calculated blood loss in vaginal and cesarean delivery. Am J Obstet Gynecol 2008; 199: 519.
26. Nadler SB, Hidalgo JH, Bloch T. Prediction of blood volume in normal human adults. Surgery 1962; 51: 224–32.
27. Pearson TC, Guthrie DL, Simpson J, et al. Interpretation of measured red cell mass and plasma volume in adults: Expert Panel on Radionuclides of the International Council for Standardization in Haematology. Br J Haematol 1995; 89: 748–56.
28. Bourke DL, Smith TC. Estimating allowable hemodilution. Anesthesiology 1974; 41: 609–12.
29. Gross JB. Estimating allowable blood loss: corrected for dilution. Anesthesiology 1983; 58: 277–80.
30. Mercuriali F, Inghilleri G. Proposal of an algorithm to help the choice of the best transfusion strategy. Curr Med Res Opin 1996; 13: 465–78.
31. Camarasa MA, Ollé G, Serra-Prat M, et al. Efficacy of aminocaproic, tranexamic acids in the control of bleeding during total knee replacement: a randomized clinical trial. Br J Anaesth 2006; 96: 576–82.
32. López-Picado A, Albinarrate A, Barrachina B. Determination of perioperative blood loss: accuracy or approximation? Anesth Analg 2017; 125: 280–6.
33. ICSH. Recommendations for Haemoglobinometry in Human Blood. Br J Haematol 1967; 13: suppl. 71–6.
34. Konig G, Holmes AA, Garcia R, et al. In vitro evaluation of a novel system for monitoring surgical hemoglobin loss. Anesth Analg 2014; 119: 595–600.
35. Sharareh B, Woolwine S, Satish S, Abraham P, Schwarzkopf R. Real Time intraoperative monitoring of blood loss with a novel tablet application. Open Orthop J 2015; 9: 422–6.
36. Fedoruk K, Seligman KM, Carvalho B, Butwick AJ. Assessing the association between blood loss and postoperative hemoglobin after cesarean delivery: a prospective study of 4 blood loss measurement modalities. Anesth Analg 2019; 128: 926–32.
37. Saoud F, Stone A, Nutter A, Hankins GD, Saade GR, Saad AF. Validation of a new method to assess estimated blood loss in the obstetric population undergoing cesarean delivery. Am J Obstet Gynecol 2019; 221: 267.
38. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004; 240: 205–13.

Current Diagnosis and Management of Acute Pulmonary Embolism: A Strategy for General Practitioners in Emergency Department

Joshua Eldad Frederich Lasanudin[1], Sidhi Laksono[2,3,*], Hillary Kusharsamita[4]

ABSTRACT

Pulmonary embolism (PE) is a disease with a relatively good prognosis when diagnosed and treated properly. This review aims to analyse available data and combine them into algorithms that physicians can use in the emergency department for quick decision-making in diagnosing and treating PE. The available data show that PE can be excluded through highly sensitive clinical decision rules, i.e. Pulmonary Embolism Rule-Out Criteria (PERC), Wells criteria, and Revised Geneva criteria, combined with D-dimer assessment. In cases where PE could not be excluded through the mentioned strategies, imaging modalities, such as compression ultrasonography (CUS), computed tomographic pulmonary angiography (CTPA), and planar ventilation/perfusion (V/Q) scan, are indicated for a definite diagnosis. Once a diagnosis has been made, treatment of PE depends on its mortality risk as patients are divided into low-, intermediate-, and high-risk cases. High-risk cases are treated for their hemodynamic instability, given parenteral or oral anticoagulant therapy, and are indicated for reperfusion therapy. Intermediate-risk PE is only given parenteral or oral anticoagulants and reperfusion is indicated when anticoagulants fail. Low-risk cases are given oral anticoagulants and based on the Hestia criteria, patients may be discharged and treated as outpatients.

AUTHOR AFFILIATIONS

[1] Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia
[2] Department of Cardiology and Vascular Medicine, Central Pertamina Hospital, Jakarta, Indonesia
[3] Faculty of Medicine, Universitas Muhammadiyah Prof Dr Hamka, Tangerang, Indonesia
[4] Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia
* Corresponding author: Fakultas Kedokteran Universtas Muhammadiyah Prof Dr Hamka, Jl. Raden Patah No.01, RT.002/RW.006, Parung Serab, Kec. Ciledug, Kota Tangerang, Banten 13460, Indonesia; e-mail: sidhilaksono@uhamka.ac.id

INTRODUCTION

Pulmonary embolism is a blockage of the lung vasculature by embolic venous thrombi. The exact global incidence of pulmonary embolism is unknown, but large surveys within countries have estimated that, annually, pulmonary embolism occurs at approximately 1 in 1000 persons (1, 2). However, this true incidence of the disease may be larger as post-mortem studies have shown that pulmonary embolism is found as the mechanism of death in around 5–10% of cases (3–5). Furthermore, in many cases in which an autopsy reveals pulmonary embolism as the cause of death, the diagnosis was never made clinically (5–6). Hence, a high index of suspicion for the disease along with proper steps in diagnosing pulmonary embolism is needed.

Additionally, it should be noted that the overall prognosis of pulmonary embolism is good, with studies generally showing mortality rates of under 10% (7). However, such studies mostly assess diagnosed and, hence, treated pulmonary embolism cases. A review by Cohen et al. reveals that of all pulmonary embolism-related death, 59% were from undiagnosed and untreated cases, whereas only 7% were from those properly diagnosed and treated (8). These findings suggests that adequate treatment results in a better prognosis and further supports the need of a proper strategy in diagnosing and managing patients with pulmonary embolism.

DIAGNOSIS OF PULMONARY EMBOLISM

Diagnosing pulmonary embolism starts from the clinical signs and symptoms of the patient. A meta-analysis by West et al. shows that from clinical history, pulmonary embolism has a high likelihood ratio if the patient presents with syncope, current deep vein thrombosis (DVT), leg swelling, sudden dyspnea, active cancer, recent surgery, hemoptysis, or leg pain. On the other hand, rarely does a pulmonary embolism present without sudden dyspnea and tachypnea. A systematic review conducted by Stein, et al. found silent PE diagnosed in 1665 of 5233 patients (32%) with DVT. It was higher found in proximal DVT rather than distal DVT (9).

From physical examination, patients with shock have a high likelihood of pulmonary embolism (10). Moreover, the use of clinical features as a basis for judgement to rule in or rule out pulmonary embolism is made more sensitive and specific through scoring tools. Commonly used tools include the pulmonary embolism rule-out criteria (PERC), Wells score, Revised Geneva score, Simplified Geneva score, and the YEARS algorithm (11).

The American College of Physcians released guidelines for ruling out pulmonary embolism using said scoring methods as follow (12):

1. Should all physicians assest and decide probability of PE (low, intermediate, high) using either a clinical decision tool or gestalt.
2. Wells or Geneva Score are used to determine patient's risk for PE.

3. In low-risk probability of PE patient, PERC are reccomended. When the PERC scoring are negative, no further test is needed, and PE can be ruled out. When the PERC score are positive, do high-sensitivity plasma D-dimer test as initial test.
4. Patient with intermediate risk can underwent plasma D-dimer test, PERC are not necessary.
   a. Patient > 50 years use an age-adjusted threshold (age × 10ng/mL) as D-dimer increased with age.
   b. D-dimer lower than treshold no need further imaging test.
   c. Patient with raised D-dimer should do imaging test.
5. Patient with high risk of PE should skip the D-dimer test and underwent imaging studies.
   a. CTPA are reccomended when there is no contra-indication.
   b. V/Q lung scanning can be used when CTPA is unavailable or contraindicated.

The Wells score assesses seven factors and associates each factor with a certain point (Table 1). There were 3 tier (low, moderate, or higher) or 2 tier (likely or unlikely) models that physician can use. In three tier model, score 0–1 are considered low, score 2–6 are considered moderated, while >6 are considered high. In two tier model otherwise, <4 score are unlikely, while ≥4 score are likely (13). A meta-analysis by Bass et al. reveals that the sensitivity and specificity of the criteria ranges from 60% to 70% and from 60% to 80% respectively (14, 15). Further, in the original study by Wells et al., the combination of a low probability Wells criteria alongside a negative D-dimer testing was found to have a negative predictive value of 99.5% (16). A meta-analysis supports the notion that combining Wells criteria and D-dimer testing increases sensitivity to 99.7%, although the specificity decreases dramatically (15). This indicates that performing Wells criteria alone is likely insufficient, which other scoring tools should be considered. ESC also recommending Wells score supported by D-dimer results to rule out PE (17).

The revised Geneva score is another clinical decision tool for the diagnostic workup of patients suspected with pulmonary embolism. It consists of nine variables, and each are given points accordingly (Table 2). If the accumulation of points results in 11 or higher, then the patient has a high probability of pulmonary embolism (18). The scoring was further simplified so that each item were given

Tab. 1 Wells score (11, 13).

Factors assessed	Points
An alternative diagnosis is less likely than pulmonary embolism	3.0
Clinical signs and symptoms of deep vein thrombosis (DVT)	3.0
Tachycardia (heart rate > 100 beats/min)	1.5
Immobilization or surgery in previous four weeks	1.5
Previous DVT or pulmonary embolism	1.5
Hemoptysis	1.0
Active malignancy	1.0

Tab. 2 Revised and simplified Geneva Score (11, 18, 19).

Factors assessed	Points (Revised)	Points (Simplified)
Age > 65 years	1	1
Previous DVT or pulmonary embolism	3	1
Surgery or fracture within 1 month	2	1
Active malignant condition	2	1
Unilateral lower limb pain	3	1
Hemoptysis	2	1
Heart rate of 75–94 beats/min	3	1
Heart rate of 95 beats/min or more	5	2
Pain on lower-limb deep venous palpation and unilateral edema	4	1

Tab. 3 D-dimer cut-offs (25).

D-dimer test	Defined as negative if D-dimer level is …
Qualitative test	Shown negative on device
Fixed cut-off	< 500 ng/mL
Age-adjusted cut-off	Patients < 50 years old: < 500 ng/mL
	Patients ≥ 50 years old: < (age × 10) ng/mL
Pre-test-probability-adjusted cut-off	Wells criteria ≤ 4: < 1000 ng/mL Wells criteria ≤ 6: < 500 ng/mL
	Revised Geneva criteria ≤ 5: < 1000 ng/mL Revised Geneva criteria ≤ 10: < 500 ng/mL

one point, excluding heart rate ≥ 95 beats/min which is given two points, and a result of more than and equal to five indicates a high probablity of pulmonary embolism. It was found that the simplification of the scoring system does not affect its diagnostic value (19). Further studies have shown that a revised Geneva score of 10 or less when combined with a negative D-dimer test have a sensitivity of nearly 100% (20, 21). Hence, exclusion of pulmonary embolism in such circumstances can be supported.

The PERC criteria comprises of an eight-item questionnaire, which are (22, 23):

1. Is the patient's age ≥ 50 years old?
2. Is the patient's heart rate ≥ 100 times per minute?
3. Is the pulse oxymetry reading < 95% while on room air?
4. Is there hemoptysis?
5. Is the patient taking exogenous estrogen?
6. Is there a prior history of venous thromboembolism diagnosis?
7. Has the patient had recent surgery or trauma within the last 4 weeks?
8. Does the patient have swelling in one leg?

If all questions are answered as 'no', it is regarded as PERC negative, whereas if one or more questions are answered as 'yes', it is regarded as PERC positive. A negative PERC criteria when combined with a low initial clinical suspicion of pulmonary embolism, i.e. a physician's implicit estimation of pulmonary embolism is less than 15%, reduces the probability of venous thromboembolism to less than 2% (22). Thus, pulmonary embolism can be ruled out in such cases.

The YEARS clinical decision rule combines both presenting clinical manifestations and D-dimer values. Patients are clinically assessed for the following items: clinical signs of DVT, the presence of hemoptysis, and whether pulmonary embolism is the most likely diagnosis. In patients with none of the abovementioned items and a D-dimer less than 1000 ng/mL, pulmonary embolism can be excluded. On the other hand, patients with one or more items, a D-dimer less than 500 ng/mL supports the exclusion of pulmonary embolism (24). A meta-analysis by Geersing et al. reveals that the sensitivity and specificity of the YEARS algorithm in primary healthcare is 98.2% and 60.55% respectively (25).

As has been mentioned, the addition of D-dimer testing increases sensitivity. However, besides the YEARS algorithm, the other scoring systems do not explicitly state the recommended cut-off value for D-dimer. A study by Riley, et al. shows widely used D-dimer manufacturer have their own cut-off (mostly 200 ng/mL and 500 ng/mL). Physicians and laboratorians should pay attention on what D-dimer assay they uses (26). Geersing et al. includes studies that combine the Wells criteria with a qualitative D-dimer cut-off, a fixed cut-off, an age-adjusted cut-off, or pre-test-probability-adjusted cut-off. These cut-offs are also combined with the Revised Geneva criteria (25). The definition of the cut-offs are listed in (Table 3). In all of those combinations, it is found that the sensitivity remains high, ranging from 96% to 99% (25). Hence, any combination with the aforementioned cut-offs can be used to exclude pulmonary embolism.

In cases where pulmonary embolism could not be excluded through clinical decision rules and D-dimer assessment, further testing is required. According to the European Society of Cardiology (ESC) 2019 guideline for pulmonary embolism, several imaging techniques are available to accept or reject the diagnosis of pulmonary embolism (27). The recommended imaging modalities include computed tomographic pulmonary angiography (CTPA), planar ventilation/perfusion (V/Q) scan, and compression ultrasonography (CUS) (27).

A meta-analysis reveals that CTPA has a sensitivity of 94% and a specificity of 98% (28), thus making it an excellent diagnostic modality for pulmonary embolism. A similar high sensitivity and specificity is also found in V/Q scans (28). However, both of these modalities incorporate radiation and thus proposes a risk to the patient. On the other hand, proximal vein CUS does not use radiation. This tool is used to find evidence of deep vein thrombosis and can be used as an indirect tool to diagnose pulmonary embolism. This is due to the presumption that the majority of pulmonary embolism arises from DVT. A positive finding has a sensitivity of 49% and a specificity of 96% for diagnosing pulmonary embolism (28). Another study supports the notion that in suspected patients, either clinically or through positive D-dimer testing, a positive vein CUS has a specificity of 99% (29). Thus, in such cases, CUS can be used to rule-in pulmonary embolism. An overall algorithm to diagnose pulmonary embolism is presented on Figure 1.
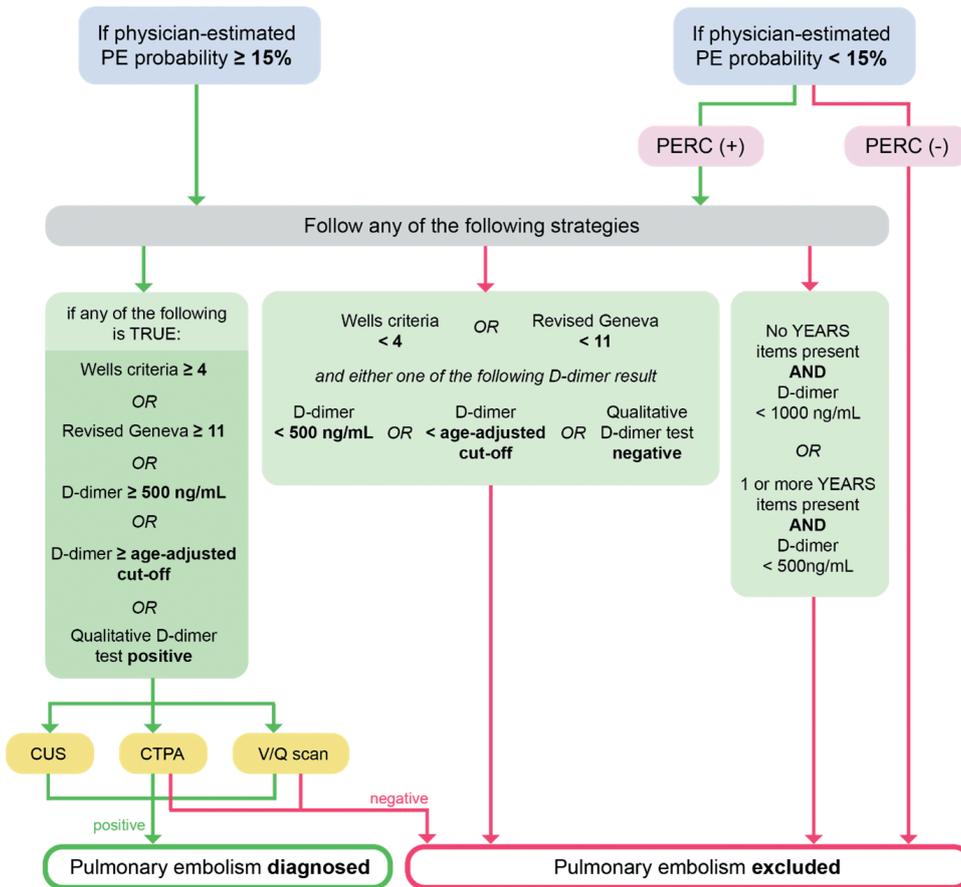
Fig. 1 Diagnostic algorithm for pulmonary embolism (11, 22, 25). Abbreviations: PE = pulmonary embolism; PERC = pulmonary embolism rule-out criteria; CUS = compression ultrasonography; CTPA = computed tomographic pulmonary angiography; V/Q scan = ventilation/perfusion scan.

MANAGEMENT OF PULMONARY EMBOLISM IN THE EMERGENCY DEPARTMENT

RISK STRATIFICATION

Pulmonary embolism management is guided by the severity of the case, which is divided into three risk categories: high, intermediate, and low. Further scoring systems have been developed to measure the prognosis of patients, the most commonly used are the Pulmonary Embolism Severity Index (PESI), which has later been simplified (27, 30, 31). These scoring assess multiple factors and each factor are coupled with a certain weighted point. Higher accumulation of points indicates more severe cases, i.e. a higher risk of death within 30 days (30, 31). Both the original and simplified versions of the PESI, along with their interpretations, can be found in (Table 4).

In stratifying patients into high-, intermediate-, and low-risk pulmonary embolism, a combination of the PESI or simplified PESI (sPESI) score, along with findings of hemodynamic instability, right ventricular dysfunction, and elevation of cardiac troponin levels are incorporated. Hemodynamic instability is defined as at least one of the following clinical presentation: (1) cardiac arrest, (2) obstructive shock (systolic blood pressure < 90 mmHg or requirement of vasopressors to maintain blood pressure ≥ 90 mmHg despite adequate filling status, along with findings of end-organ hypoperfusion), or (3) persistent

hypotension (systolic blood pressure < 90 mmHg or systolic blood pressure drops by ≥ 40 mmHg, lasts > 15 minutes, and not caused by new-onset arrhythmia, sepsis, or hypovolemia). Right ventricular dysfunction can be detected through transthoracic echocardiography or CTPA (27).

A high-risk pulmonary embolism is characterised by hemodynamic instability. In intermediate-risk pulmonary embolism, the patient is hemodynamically stable, but PESI or sPESI are > 85 or ≥ 1, respectively. This can also be combined with findings of right ventricular dysfunction or elevated cardiac troponin levels. In low-risk pulmonary embolism, none of the above parameters are found (27). Table 5 provides a summary of the stratification of pulmonary embolism mortality risk.

MANAGEMENT OF HIGH-RISK PULMONARY EMBOLISM

Initial management for high-risk pulmonary embolism include respiratory support and hemodynamic correction. Respiratory support is indicated in patients with oxygen saturation less than 90%. Oxygen therapy can be given through high-flow nasal cannula (HFNC) or mechanical ventilation (27). The use of HFNC is found to increase oxygen saturation and decrease respiratory rate in a couple of hours after initiation (32, 33). Further, its use is found to be superior to that of conventional nasal cannula (32).

Tab. 4 Pulmonary Embolism Severity Index (30, 31).

Factor assessed	Original version	Simplified version
Age	Age in years = points	1 point (if > 80 years)
Male	+ 10 points	–
Cancer	+ 30 points	1 point
Chronic heart failure	+ 10 points	1 point
Chronic pulmonary disease	+ 10 points	
HR ≥ 110 beats/minute	+ 20 points	1 point
Systolic BP < 100 mmHg	+ 30 points	1 point
RR > 30 breaths/minute	+ 20 points	–
Temperature < 36 °C	+ 20 points	–
Altered mental status	+ 60 points	–
Arterial oxyhemoglobin saturation < 90%	+ 20 points	1 point
Interpretation	Point accumulation	Point accumulation
	• ≤ 65: very low 30-day mortality risk (0–1.6%) • 66–85: low 30-day mortality risk (1.7–3.5%) • 86–105: moderate 30-day mortality risk (3.2–7.1%) • 106–125: high 30-day mortality risk (4.0–11.4%) • > 125: very high 30-day mortality risk (10–24.5%)	• 0: 30-day mortality risk 1% • ≥ 1: 30-day mortality risk 10.9%

Abbreviations: HR = heart rate; RR = respiratory rate

Tab. 5 Stratification of pulmonary embolism severity (27).

Risk	Indicators			
	Hemodynamic instability	PESI > 85 or sPESI ≥ 1	RV dysfunction	Elevated cardiac troponin levels
High	+	+	+	+
Intermediate	–	+	+/–	+/–
Low	–	–	–	–

Abbreviations: PESI = Pulmonary Embolism Severity Index; sPESI = simplified Pulmonary Embolism Severity Index; RV = right ventricular.

Non-invasive mechanisms should be attempted first and intubation is reserved for refractory cases (27).

Hemodynamic instability due to acute right ventricular failure can be treated by increasing volume and/or the use of vasopressors. A ≤ 500 mL fluid challenge can be given in cases where central venous pressure is low (27, 34). However it should be noted that excessive fluid may cause further deterioration of right ventricular function as it increases wall stress and induces further ischemia (35). Pharmacological approach through vasopressors and inotropes can also be considered. The ESC guideline recommends the use of norepinephrine, 0.2–1.0 mcg/kg/minute, and/or dobutamine, 2–20 mcg/kg/minute (27). If dobutamine is used, it is recommended to also incorporate

Tab. 6 Hestia exclusion criteria (11, 27).

Questions
Is the patient haemodynamically unstable?
Is reperfusion therapy necessary?
Is there an active bleeding or high risk of bleeding?
Does the patient need > 24 hour of oxygen supply to maintain oxygen saturation > 90%?
Is pulmonary embolism diagnosed while patient is taking anticoagulant treatment?
Is there severe pain which needs intravenous pain medication for > 24 hours?
Medical or social reason for treatment in the hospital for >24 hours (infection, malignancy, or no support system)?
Does the patient have a creatinine clearance of <30 mL/min?
Does the patient have severe hepatic impairment?
Is the patient pregnant?
Is there a documented history of heparin-induced thrombocytopenia?

norepinephrine as dobutamine has a vasodilatory effect that could cause further hypotension (27, 36). On the other hand, norepinephrine can be given as a monotherapy (37).

Further, in patients with a high clinical probability of pulmonary embolism (refer to the Wells or Geneva mentioned on the previous section), initial anticoagulation can be administered even before the results of diagnostic tests. Parenteral anticoagulation is the recommended approach and patients are administered subcutaneous low-molecular weight heparin (LMWH; e.g., enoxaparin 1 mg/kg every 12 hours) or fondaparinux (7.5 mg once daily for patients weighing 50–100 kg) or intravenous unfractionated heparin (UFH) (27). Studies have found that LMWH and fondaparinux have a lower risk for bleeding compared to UFH (38–40). Moreover, the efficacy of LMWH and fondaparinux are similar to that of UFH (38–40). Other options that can be considered include non-vitamin K antagonist oral anticoagulants and vitamin K antagonists (27).
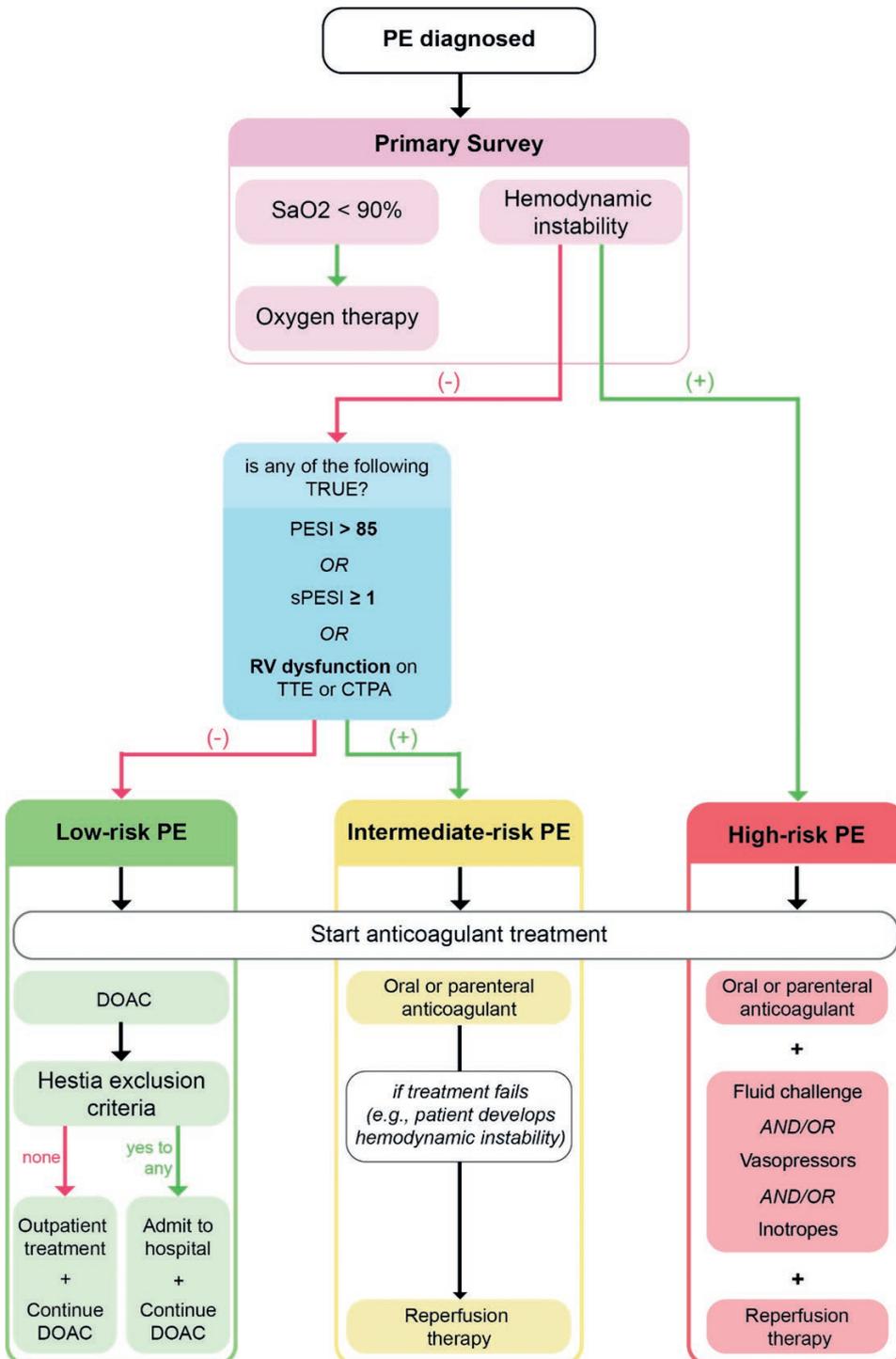
Fig. 2 Initial management of pulmonary embolism based on risk stratification (11, 27). Abbreviation: PE = pulmonary embolism; SaO2 = oxygen saturation; PESI = Pulmonary Embolism Severity Index; sPESI = simplified Pulmonary Embolism Severity Index; RV = right ventricular; DOAC = direct oral anticoagulant.

The primary treatment for high-risk pulmonary embolism is reperfusion. The mainstay of treatment is systemic thrombolysis. However, a percutaneous catheter approach and a surgical embolectomy are also viable options. A couple of meta-analyses found that, in acute pulmonary embolism which includes high-risk pulmonary embolisms, systemic thrombolysis was found to reduce mortality when compared to the use of UFH alone (41, 42). However, studies also found increased risk of major bleeding in patients who underwent systemic thrombolysis (41, 42).

Thrombolysis is optimally given within 48 hours post-onset, but can still be beneficial up to 2 weeks after onset of symptoms (27). Several approved thrombolytic regimens include recombinant tissue-type plasminogen activator (rtPA; 100 mg over 2 hours), streptokinase (250,000 IU loading dose for 30 minutes, continued by 100,000 IU/hour for 12–24 hours), and urokinase (4,400 IU/kg loading dose for 10 minutes, followed by 4,400 IU/kg/hour over 12–24 hours) (27). It should be noted that before undergoing systemic thrombolysis, contraindications must be assessed (e.g., active bleeding, history of stroke, intracranial neoplasm) (27, 43). Surgical pulmonary embolectomy and percutaneous catheter-directed treatment is reserved for cases where systemic thrombolysis is contraindicated or has failed (27).

MANAGEMENT OF INTERMEDIATE-RISK PULMONARY EMBOLISM

In intermediate-risk pulmonary embolism, anticoagulation treatment, whether orally or parenterally, along with hospitalisation for monitoring is usually sufficient (27). Routine thrombolytic therapy is not recommended and it is only performed in patients who develop hemodynamic instability (27). A trial by Meyer et al. shows that in intermediate-risk pulmonary embolism, thrombolytic therapy increases the risk of major bleeding and stroke when compared to treatment with anticoagulation alone (44). However, other studies have also shown that catheter-directed thrombolysis are as safe as anticoagulation treatment only and is able to improve patients' condition (marked by improvement of hemodynamic parameters) (45–47). Nonetheless, in the long term, no difference in mortality between catheter-directed thrombolysis and anticoagulation treatment alone is found (45).

MANAGEMENT OF LOW-RISK PULMONARY EMBOLISM

Low-risk pulmonary embolism are treated by administration of direct oral anticoagulant therapy (11, 27). A further decision that needs to be made in low-risk populations is whether hospitalization is necessary or if patients can be discharged early (27). Several studies have shown that low-risk patients can be safely and effectively treated as outpatients using direct oral anticoagulants (48, 49). However, it is recommended to further stratify low-risk patients using the Hestia exclusion criteria, which consists of 11 criterion (Table 6). If any of the questions asked is answered 'yes', then the patient should be hospitalised (27, 50).

MANAGEMENT IN SPECIFIC POPULATION

In pregnant patient, CUS can be considered in order to avoid radiation. Perfusion scintigraphy in pregnant patient with normal chest X-ray to rule out PE. LMWH are recommended during pregnancy without shock or hypotension. For patient with cancer who diagnosed with PE, subcutaneous LMWH are recommended for first 3–6 month, except for high-risk PE. After then, LMWH still can be continued, switched to VKA, or discontinued. This decision should be made carefully after considering the success of anti-cancer therapy, risk of recurrence of VTE, bleeding risk, and patient's preference (17).

CONCLUSION

Patients with pulmonary embolism that comes into the emergency department, when diagnosed and treated in a timely manner, have a good prognosis. There is a breadth of clinical manifestations related to the disease which has further been simplified into scoring systems, i.e. PERC, Wells criteria, or Revised Geneva criteria, that can be utilised to exclude and diagnose pulmonary embolism. The initial supporting test needed is D-dimer, whereas imaging modalities are reserved in cases where pulmonary embolism still can't be excluded after clinical and D-dimer tests. Treatment of pulmonary embolism is based on risk stratification into high-, intermediate-, and low-risk cases. Hemodynamic status along with oxygen saturation should be corrected and anticoagulants are given to every case. Reperfusion therapy is only mandated in high-risk cases and are given in other risk groups only if anticoagulants fail or contraindicated. In low-risk cases, consider early discharge for patients that fulfil the Hestia criteria.

ACKNOWLEDGEMENTS

REFERENCES

1. Andersson T, Söderberg S. Incidence of acute pulmonary embolism, related comorbidities and survival; analysis of a Swedish national cohort. BMC Cardiovasc Disord 2017 Dec; 17(1): 155.
2. Silverstein MD, Heit JA, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ. Trends in the incidence of deep vein thrombosis and pulmonary embolism: a 25-year population-based study. Arch Intern Med 1998; 158(6): 585–93.
3. Sweet PH, Armstrong T, Chen J, Masliah E, Witucki P. Fatal pulmonary embolism update: 10 years of autopsy experience at an academic medical center. JRSM Short Rep 2013; 4(9): 2042533313489824.
4. Sandler DA, Martin JF. Autopsy proven pulmonary embolism in hospital patients: are we detecting enough deep vein thrombosis? J R Soc Med 1989; 82(4): 203–5.
5. Stein PD, Henry JW. Prevalence of acute pulmonary embolism among patients in a general hospital and at autopsy. Chest 1995; 108(4): 978–81.
6. Yun JL, Li XY. Prevalence of pulmonary embolism at autopsy among elderly patients in a Chinese general hospital. J Geriatr Cardiol 2016; 13(11): 894–8.
7. Douketis JD. Prognosis in pulmonary embolism. Curr Opin Pulm Med 2001; 7(5): 354–9.
8. Cohen A, Agnelli G, Anderson F, et al. Venous thromboembolism (VTE) in Europe: The number of VTE events and associated morbidity and mortality. Thromb Haemost 2007; 98(10): 756–64.

9. Stein PD, Matta F, Musani MH, Diaczok B. Silent Pulmonary Embolism in Patients with Deep Venous Thrombosis: A Systematic Review. Am J Med 2010; 123(5): 426–31.

10. West J, Goodacre S, Sampson F. The value of clinical features in the diagnosis of acute pulmonary embolism: systematic review and meta-analysis. QJM 2007; 100(12): 763–9.

11. Kahn SR, de Wit K. Pulmonary Embolism. Solomon CG, editor. N Engl J Med 2022; 387(1): 45–57.

12. Raja AS, Greenberg JO, Qaseem A, Denberg TD, Fitterman N, Schuur JD. Evaluation of Patients with Suspected Acute Pulmonary Embolism: Best Practice Advice from the Clinical Guidelines Committee of the American College of Physicians. Ann Intern Med 2015; 163(9): 701–11.

13. Gibson NS, Sohne M, Kruip MJHA, et al. Further validation and simplification of the Wells clinical decision rule in pulmonary embolism. Thromb Haemost 2008; 99(1): 229–34.

14. Lucassen W, Geersing GJ, Erkens PMG, et al. Clinical Decision Rules for Excluding Pulmonary Embolism: A Meta-analysis. Ann Intern Med 2011; 155(7): 448.

15. Bass A, Fields K, Goto R, Turissini G, Dey S, Russell L. Clinical Decision Rules for Pulmonary Embolism in Hospitalized Patients: A Systematic Literature Review and Meta-analysis. Thromb Haemost 2017; 117(11): 2176–85.

16. Wells PS, Anderson DR, Rodger M, et al. Excluding Pulmonary Embolism at the Bedside without Diagnostic Imaging: Management of Patients with Suspected Pulmonary Embolism Presenting to the Emergency Department by Using a Simple Clinical Model and d-dimer. Ann Intern Med 2001; 135(2): 98.

17. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J 2020; 41(4): 543–603.

18. Le Gal G, Righini M, Roy PM, et al. Prediction of Pulmonary Embolism in the Emergency Department: The Revised Geneva Score. Ann Intern Med 2006; 144(3): 165.

19. Klok FA, Mos ICM, Nijkeuter M, et al. Simplification of the Revised Geneva Score for Assessing Clinical Probability of Pulmonary Embolism. Arch Intern Med 2008; 168(19): 2131.

20. Can Z, Danjie G. Predictive values of the Wells and Revised Geneva scores combined with D-dimer for suspected pulmonary embolism in elderly patients. Heart 2012; 98(Suppl 2): E279.3–E280.

21. Carrier M, Righini M, Djurabi RK, et al. VIDAS D-Dimer in Combination with Clinical Pre-Test Probability to Rule out Pulmonary Embolism. A Systematic Review of the Management Outcome Studies. Blood 2008; 112(11): 1811.

22. Kline JA, Courtney DM, Kabrhel C, et al. Prospective multicenter evaluation of the pulmonary embolism rule-out criteria: Prospective multicenter evaluation of the PERC. J Thromb Haemost 2008; 6(5): 772–80.

23. Kline JA, Mitchell AM, Kabrhel C, Richman PB, Courtney DM. Clinical criteria to prevent unnecessary diagnostic testing in emergency department patients with suspected pulmonary embolism. J Thromb Haemost 2004; 2(8): 1247–55.

24. van der Hulle T, Cheung WY, Kooij S, Beenen LFM, et al. Simplified diagnostic management of suspected pulmonary embolism (the YEARS study): a prospective, multicentre, cohort study. Lancet 2017; 390(10091): 289–97.

25. Geersing GJ, Takada T, Klok FA, et al. Ruling out pulmonary embolism across different healthcare settings: A systematic review and individual patient data meta-analysis. Basu S, editor. PLoS Med 2022; 19(1): e1003905.

26. Riley RS, Gilbert AR, Dalton JB, Pai S, McPherson RA. Widely Used Types and Clinical Applications of D-Dimer Assay. Lab Med 2016; 47(2): 90–102.

27. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J 2020; 41(4): 543–603.

28. Patel P, Patel P, Bhatt M, et al. Systematic review and meta-analysis of test accuracy for the diagnosis of suspected pulmonary embolism. Blood Adv 2020; 4(18): 4296–311.

29. Le Gal G, Righini M, Sanchez O, et al. A positive compression ultrasonography of the lower limb veins is highly predictive of pulmonary embolism on computed tomography in suspected patients. Thromb Haemost 2006; 95(6): 963–6.

30. Aujesky D, Obrosky DS, Stone RA, et al. Derivation and validation of a prognostic model for pulmonary embolism. Am J Respir Crit Care Med 2005; 172(8): 1041–6.

31. Jiménez D, Aujesky D, Moores L, et al. Simplification of the pulmonary embolism severity index for prognostication in patients with acute symptomatic pulmonary embolism. Arch Intern Med 2010; 170(15): 1383–9.

32. Aksakal A, Sağlam L, Kerget B, Yılmazel Uçar E. Comparison of the effectiveness of high-flow and conventional nasal cannula oxygen therapy in pulmonary embolism patients with acute hypoxemic respiratory failure. Tuberk Toraks 2021;69(4) :469–76.

33. Messika J, Goutorbe P, Hajage D, Ricard JD. Severe pulmonary embolism managed with high-flow nasal cannula oxygen therapy. Eur J Emerg Med 2017 Jun; 24(3): 230–2.

34. Mercat A, Diehl JL, Meyer G, Teboul JL, Sors H. Hemodynamic effects of fluid loading in acute massive pulmonary embolism. Crit Care Med 1999; 27(3): 540–4.

35. Wood KE. Major Pulmonary Embolism. Chest 2002; 121(3): 877–905.

36. Sekhri V, Mehta N, Rawat N, Lehrman SG, Aronow WS. State of the art paper Management of massive and nonmassive pulmonary embolism. Arch Med Sci 2012; 6: 957–69.

37. Kucher N, Goldhaber SZ. Management of Massive Pulmonary Embolism. Circulation 2005;112(2): e28–32.

38. Büller HR, Gent M, Gallus AS, Ginsberg J, Prins MH, Baildon R. Low-Molecular-Weight Heparin in the Treatment of Patients with Venous Thromboembolism. N Engl J Med 1997; 337(10): 657–62.

39. Hull RD. Low-Molecular-Weight Heparin vs Heparin in the Treatment of Patients with Pulmonary Embolism. Arch Intern Med 2000; 160(2): 229.

40. Simonneau G, Sors H, Charbonnier B, et al. A Comparison of Low-Molecular-Weight Heparin with Unfractionated Heparin for Acute Pulmonary Embolism. N Engl J Med 1997; 337(10): 663–9.

41. Marti C, John G, Konstantinides S, Combescure C, et al. Systemic thrombolytic therapy for acute pulmonary embolism: a systematic review and meta-analysis. Eur Heart J 2015; 36(10): 605–14.

42. Chatterjee S, Chakraborty A, Weinberg I, et al. Thrombolysis for Pulmonary Embolism and Risk of All-Cause Mortality, Major Bleeding, and Intracranial Hemorrhage: A Meta-analysis. JAMA 2014; 311(23): 2414.

43. Yilmazel Ucar E. Update on Thrombolytic Therapy in Acute Pulmonary Thromboembolism. Eurasian J Med 2019; 51(2): 185–9.

44. Meyer G, Vicaut E, Danays T, et al. Fibrinolysis for Patients with Intermediate-Risk Pulmonary Embolism. N Engl J Med 2014; 370(15): 1402–11.

45. Kucher N, Boekstegers P, Müller OJ, et al. Randomized, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism. Circulation 2014; 129(4): 479–86.

46. Engelberger RP, Moschovitis A, Fahrni J, et al. Fixed low-dose ultrasound-assisted catheter-directed thrombolysis for intermediate and high-risk pulmonary embolism. Eur Heart J 2015; 36(10): 597–604.

47. Kuo WT, Banerjee A, Kim PS, et al. Pulmonary Embolism Response to Fragmentation, Embolectomy, and Catheter Thrombolysis (PERFECT): Initial Results from a Prospective Multicenter Registry. Chest 2015; 148(3): 667–73.

48. Bledsoe JR, Woller SC, Stevens SM, et al. Management of Low-Risk Pulmonary Embolism Patients Without Hospitalization. Chest 2018; 154(2): 249–56.

49. Maughan BC, Frueh L, McDonagh MS, Casciere B, Kline JA. Outpatient Treatment of Low-risk Pulmonary Embolism in the Era of Direct Oral Anticoagulants: A Systematic Review. Courtney M, editor. Acad Emerg Med 2021; 28(2): 226–39.

50. Zondag W, Mos ICM, Creemers-Schild D, Hoogerbrugge ADM, et al. Outpatient treatment in patients with acute pulmonary embolism: the Hestia Study. J Thromb Haemost 2011; 9(8): 1500–7.

The Evaluation of Training Oral and Maxillofacial Trainees in Head and Neck Cancer Doctor-Patient Communication Using the Patient Concerns Inventory

Emma G. Walshaw[1], Simon Rogers[2], Jianhua Wu[3], John Sandars[4], Anastasios Kanatas[5,*]

ABSTRACT

Head and neck cancer has a significant impact on a patient's health related quality of life (HRQOL). The head and neck specific Patient Concerns Inventory (PCI-HN) has been utilised to enhance doctor-patient dialogue in routine consultations. To date there has been no formal training for oral and maxillofacial surgery (OMFS) surgical trainees in the use of the PCI-HN in consultations. The aim of the study was to evaluate training for OMFS surgical trainees in the use of the PCI-HN, using simulated follow-up HNC consultations, in order to improve doctor-patient communication skills.

Material and methods: Ten oral and maxillofacial surgical trainees completed actor simulated HNC consultations before and after training. A study-specific mark scheme was developed based on the ComOn-Coaching rating scales and used to score the doctor-patient interaction. A group debrief afterwards explored the trainee's experiences of the training and consultations.

Results: All trainees showed an improvement in doctor-patient communication scores following their training. Overall, the six participants who were Specialty registrars, year 3 (ST3) or above, scored higher, than the four Specialty registrars, year 1–2 (ST1-2). The scores were higher if fewer PCI-HN items were discussed (3–4). The most frequently avoided PCI-HN items were intimacy and relationships. The trainees considered that their training was useful for organising their consultations and for providing holistic care.

Conclusion: Although training improved surgeon-patient communication, further evaluation is required with a larger number of trainees and actual consultations in clinic.

KEYWORDS

head and neck cancer; clinical training; Oral and Maxillofacial; Patient Concerns Inventory; surgeon-patient communication

AUTHOR AFFILIATIONS

[1] Bradford Teaching Hospitals NHS Trust, BD9 6DA, United Kingdom
[2] Maxillofacial Department, Wirral University Teaching Hospital, Wirral, CH49 5PE, United Kingdom
[3] School of Dentistry, University of Leeds, UK and Wolfson Institute of Population Health, Queen Mary University of London, United Kingdom
[4] Edgehill University, St Helens Rd, Ormskirk L39 4QP, United Kingdom
[5] Leeds Teaching Hospitals and St James Institute of Oncology, Leeds Dental Institute and Leeds General Infirmary, LS1 3EX, United Kingdom

* Corresponding author: Leeds Teaching Hospitals and St James Institute of Oncology, Leeds Dental Institute and Leeds General Infirmary, LS1 3EX, United Kingdom; e-mail: anastasios.kanatas@nhs.net

INTRODUCTION

Health related quality of life (HRQOL) is severely impacted by the diagnosis, treatment and recovery from head and neck cancer (HNC) (1, 2). HRQOL encompasses not only physical/functional, emotional and social areas but also includes more existential considerations such as well-being, purpose and spiritual elements (1). For HNC patients, effective doctor–patient communication in consultations is of critical importance. Good patient-centred communication can reassure, provide for sharing of information, increase adherence to management plans, lead to better patient satisfaction and improve outcomes (3–5). The Royal College of Surgeons has identified effective communication with patients as a key domain in providing Good Surgical Care (6).

The PCI-HN is an established prompt tool to help elicit patient concerns in routine HNC consultations (7); it is a 56-item prompt list completed by patients prior to their HNC consultation. The PCI-HN was first published in 2009 (8), and has been shown subsequently to be feasible as a cost-effective tool that improves health-related quality of life outcomes (9, 10). The PCI-HN helps empower patients by providing a holistic tool that allows them the opportunity to raise issues they wish to talk about in their consultation (9). The possibility of the PCI-HN increasing the duration of consultations, especially in busy routine clinics, has been perceived as a potential barrier to its use by clinicians. In fact, when used by consultants, the PCI-HN made little difference to consultation length, if anything, tended to reduce it slightly overall (11).

An essential aspect of using the PCI is effective doctor-patient communication that has a patient-centred approach. This approach to consultations requires a doctor to communicate in an individualised and holistic style that is respectful and empowers the patient (12). A patient-centred focus has been shown to improve functional outcomes and HRQOL, patient satisfaction, increased adherence to management plans and perceived quality of care (13). There is recognition by oral and maxillofacial surgeons (OMFS) of the importance of further training in doctor-patient communication for HNC consultations (14). There has been no specific training for OMFS trainees in the use of the PCI-HN in HNC consultations, so we developed a novel training intervention.

The aim of the study was to evaluate the efficacy of specific doctor-patient communication skills training for OMFS surgical trainees in the use of the PCI-HN during simulated follow-up HNC consultations. We also explored the trainee's experiences of the training and consultations.

MATERIAL AND METHODS

OMFS specialist registrars across all years of training were recruited during their allocated Deanery study day which provided the training. Approval for the study was obtained from the Yorkshire Deanery. Participation in the study was voluntary and all ten registrars provided consent for audio-visual recording and were included in the study.

The training intervention had four phases:
1. Consultation with a simulated HNC patient (Scenario A or B). This provided an opportunity for the trainee to communicate in their 'normal' style.
2. A focused interactive session was led by the OMFS consultants (SR, and AK). This session consisted of (a) a discussion of the trainee's challenges concerning doctor-patient communication during follow up HNC consultations (b) a video of the use of the PCI-HN and doctor-patient during a simulated follow-up HNC consultation (c) a discussion of the importance of

A	Establish doctor-patient relationship	0	1
B	**Agenda Setting**		
	Prioritise patient choice of items for discussion	0	1
C	**Empathic communication**		
	Encourage patient's expression of thoughts and feelings	0	1
	Validate patients' thoughts and feelings	0	1
D	**Information giving**		
	Clear explanation to patient about their concern	0	1
	Awareness that patient understands explanation	0	1
E	**Action planning**		
	Provide opportunity for shared agreement on management plan	0	1
F	**Wrap up**		
	Check that all patient's concerns have been addressed	0	1
	Provide arrangements for follow up	0	1
G	Overall consultation organised and structured	0	1
	Total score		

Fig. 1 The study-specific mark scheme utilised to score simulated consultations (0 = absent, 1 = present).

doctor-patient communication with a patient-centred focus and (d) a discussion of the experiences of the consultants in the use of the PCI-HN and doctor-patient during follow-up HNC consultations.

3. Two consultations with a simulated HNC patient (Scenario C or D, followed by Scenario E or F).
4. Group debrief to allow trainees to reflect and consolidate learning from the day.

The simulated patients throughout the training day were professional actors with previous experience of undergraduate medical exams. Prior to the study day, these actors underwent virtual training in the specific needs of HNC patients, which included teaching from OMFS Consultants and real-life patients. For each Scenario, there was a specific detailed script for the simulated patient (Appendix-Scenarios used) and this included a relevant completed PCI-HN to identify the patient's concerns. All consultations were video-recorded, and the doctor-patient communication was analysed using a study specific mark scheme (Fig. 1, developed by JS and EW). The ComOn-Coaching rating scales (15), which provides a short and reliable instrument for the assessment of real consultations in oncology and is sensitive to change by training in doctor-patient communication, was adapted to align with a widely-used consultation model used in the UK (16).

Each video was scored independently by two markers and any differences were resolved by discussion to achieve consensus. The group debrief was audio-recorded and transcribed. The transcripts were coded by template analysis to identify the key themes, with illustrative quotations (17). The transcript was independently analysed by two researchers and any differences were resolved by discussion to achieve consensus.

Fig. 2 An example PCI sheet utilised by actors and trainees during this study day.

STATISTICAL ANALYSIS

The overall scores were summarised and presented as mean and standard deviation (SD), by scenario, training level and number of PCI-HN items. To investigate the impact of factors on the overall scores, linear mixed effect models were conducted using the overall scores as the dependent variable, including scenario, training level and number of PCI-HN items as independent variables. A random intercept was included to adjust for clustering effect within each trainee. Five modelling strategies were employed to assess the effect for a combination of the three factors. The coefficient estimates along with 95% confidence interval were reported from each modelling strategy. R version 4.0.3 was used for data management and analysis.
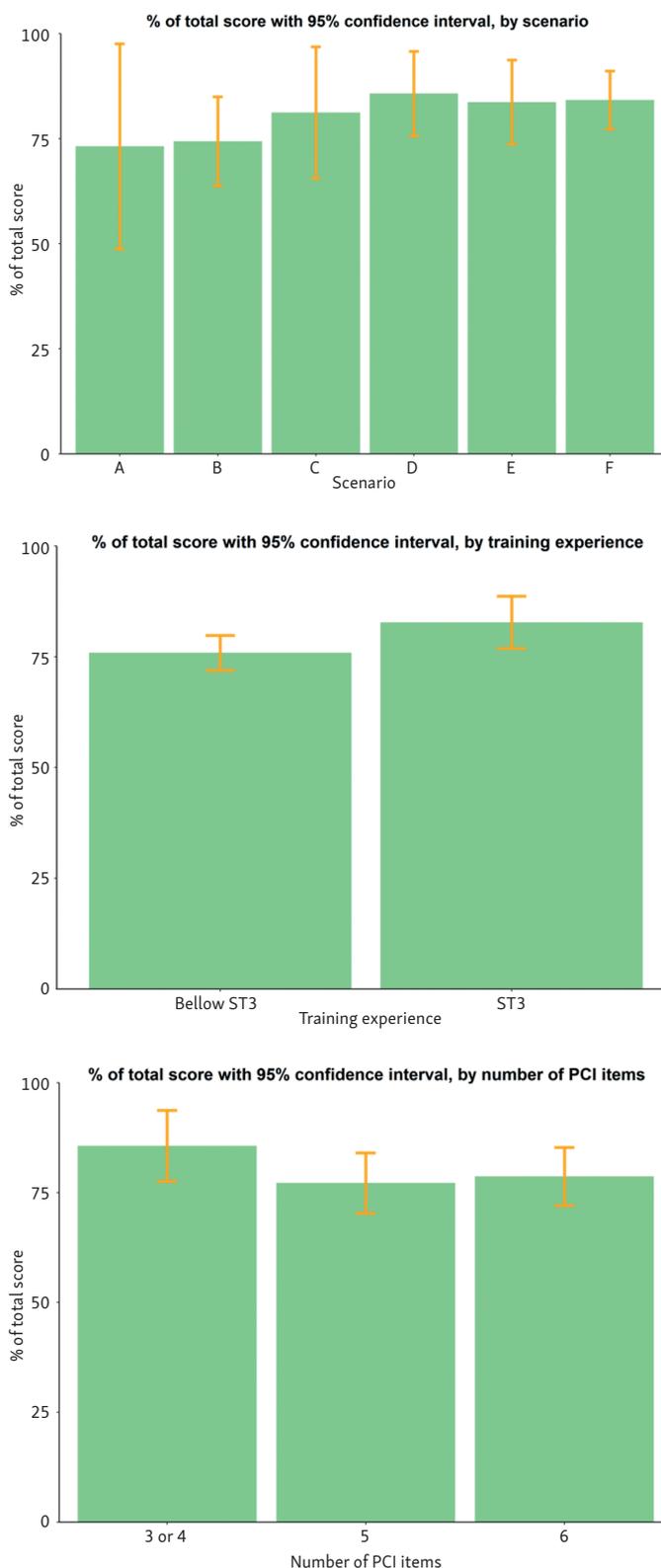
RESULTS

A total of ten trainees took part in this training day, four of whom were ST1-2, the remaining six were ST3 or above. Table 1 and Figure 3 summarise the overall consultation scores, categorised by scenario utilised, level of training and number of PCI-HN items discussed during the consultation. These results show improved scores for all trainees in scenarios following PCI-HN training (scenarios C, D, E or F). Trainees at a higher level of training (ST3 or above) also had higher scores overall. In general, those consultations where fewer PCI-HN items were explored (3–4) resulted in higher scores than those where more PCI-HN topics were covered (5–6).

The primary outcome of overall consultation score was analysed using a linear mixed effect model including factors such as scenario, training experience and number of PCI-HN items covered. The model included participants as a random intercept to adjust for clustering effect due to participants taking part in multiple scenarios. Each of

these three factors has been included in a separate model, and combined factors were investigated to assess potential impacts on overall score. The results show scenarios D, E and F resulted in higher scores in comparison to scenario A. Scenario B and C also showed improvement in comparison to scenario A, but the difference was not statistically

Fig. 3 Demonstrates overall scores categorised by scenario, training level and PCI items covered.

Tab. 1 Demonstrates overall scores categorised by scenario, training level and PCI items covered.

	Number of participants	Total score (%) (SD)
Scenario		
A	5	73.2 (19.7)
B	7	74.4 (11.5)
C	5	81.2 (12.6)
D	6	85.8 (9.6)
E	5	83.7 (8.1)
F	7	84.2 (7.5)
Training level		
Below ST3	12	75.9 (6.2)
ST3 or above	23	82.8 (13.6)
Number of PCI items		
3 or 4	12	85.6 (12.7)
5	15	77.2 (12.4)
6	8	78.7 (7.9)

Tab. 2 Coefficient estimate from different modelling strategy using linear mixed effect model.

	Coefficient estimate (95% CI)				
	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**
Scenario					
A	Reference	Reference	Reference	Reference	Reference
B	3.6 (−6.9, 14.1)			4.0 (−6.6, 14.6)	1.2 (−10.0, 12.4)
C	7.8 (−2.9, 18.5)			8.2 (−2.5, 19.0)	10.2 (−1.1, 21.5)
D	15.1 (4.4, 25.9)			15.4 (4.6, 26.2)	15.7 (4.7, 26.8)
E	13.5 (2.8, 24.1)			13.8 (3.1, 24.5)	17.4 (5.0, 29.8)
F	13.6 (3.4, 23.8)			13.7 (3.5, 23.9)	10.9 (0.03, 21.7)
Training					
Below ST3	Reference	Reference	Reference	Reference	Reference
ST3 or above		5.9 (−4.3, 16.2)		6.0 (−4.8, 16.8)	3.8 (−6.5, 14.1)
Number of PCI items					
3 or 4	Reference	Reference	Reference	Reference	Reference
5			−4.7 (−13.9, 4.5)		−6.4 (−15.6, 2.9)
6			−3.0 (−13.4, 7.4)		−9.9 (−22.0, 2.2)

significant due to the small group of participants involved (see Table 2).

The most frequently avoided items discussed during these consultations were intimacy (5) and relationships (4). Whilst work and finance (3) and pain or recurrence (2) were also avoided. Overall, 54.3% (19 of 35) scenarios had no avoided items. The simulated patients were instructed to discuss all items highlighted on their PCI-HN agenda, meaning lack of items discussed was resultant of trainees' navigation of the conversation.

The key themes identified by the group were:

(a) The PCI-HN had an impact on the trainee's organisation of their consultations:
"My initial station was kind of here and there and then you kind of pick up, you know, an organised way of how to speak to the patients and address their concerns so I felt much happier after."
"Yeah, I felt I struggled, actually. Well just because there was [sic] about 12 ticks and I was trying to …. One in the afternoon I said ok, well, there is quite a lot here we will try and get through as many as we can what are your priorities and so on."

(b) The training increased trainee's awareness of the importance of doctor-patient communication, especially patient-centredness and holistic patient care:
"I had not thought about the way patients perceive things before …"
"There is a very practical nature to doing that clinic. I think today is useful because it has reinforced all the other factors around it for some it's social and relationships."
"We don't often explore those avenues of why particularly do you think that and how do you think that so I don't know how much my patients have been missing out to be honest."

(c) The experiences and anecdotes of clinicians who regularly use the PCI-HN during doctor-patient communication was greatly valued by the participants:
"I liked the story about the shoes … he said that there was a patient who was concerned about their appearance, bought some shoes which made them feel better about themselves and I think I had not thought about the way patient's perceive things that perhaps changing their clothes could have a big impact on them."

DISCUSSION

All trainees benefited from the training, not only in consultation scores but, as revealed by the group debrief session, in an appreciation for patient concerns and how clinicians should work with patients in shared decision making about their treatment and cancer care. As expected, those further into their surgical training (ST3 or above) had a higher baseline and post-training consultation scores than more junior colleagues. This mirrors research with general surgery residents in the United States (18), and demonstrates that some background doctor-patient communication skills are learnt during surgical training regardless of specific training. However, consistent education throughout surgical training years can allow individuals to focus on different aspects of communication through time with a layered learning approach. This work provided a basis for consultation training in surgery, and it is the first time that the PCI-HN has been included in this setting.

Our study has revealed that the most frequently avoided PCI-HN items were intimacy and relationships. It is well reported that one third of patients suffering with HNC have reduced sexual interest or enjoyment after treatment (19) and specific intimacy questionnaires exist to quantify the impact on HRQOL of these concerns in HNC (20).

Lack of clinicians' knowledge about how to respond to questions regarding these topics may be to blame for the avoidance of discussion, including signposting to appropriate services. Highlighting available resources within clinics and ensuring surgeons are trained in discussing these personal items could minimise the long-term impact of these concerns and result in improved HRQOL of HNC patients and their families.

There are limitations that we must keep in mind when interpreting the results. The study included OMFS trainees from only one region (Yorkshire) and actors with different levels of experience during the simulated medical training. The study was relatively small and lacked statistical power to distinguish small differences; the actors had no previous experience with the use of the PCI-HN and it is possible that they tried to make the consultations more challenging for the trainees. Additional preparation for the mock consultations with the actors, and refinements to their simulation, would help provide a more realistic model.

The use of consented patients is worth exploring as they might provide a more accurate representation of the doctor-patient interaction. Future inclusions of trainees from other regions and specialties (including Ear, Nose and Throat surgical trainees) will allow for the development of specialty-specific training packages. It is an expectation that surgeons early in their consultant career possess a range of skills for communicating in doctor-patient consultations. Methods for assessing interpersonal communication include checklists, patient surveys and examinations (21). Checklists can be used in assessment of interactions with real or simulated patients (21). The PCI-HN has been validated in head and neck cancer patients and may provide specialty-tailored consultation training (9). Simulated clinics with real patients have been used for a long time in general practice (22) and may assist with the development of communication skills. This approach is still underdeveloped in surgical training.

The score of consultations with multiple PCI-HN items were lower than those with fewer PCI-HN items. When patients present with multiple issues, the doctor-patient interaction can be challenging. In patients with a history of treatment for head and neck cancer, there is no consensus on how to manage these challenging interactions. The General Practice policy of one issue per consultation may increase levels of stress and anger, which in turn will impact on communication (23). The trainees felt that the PCI-HN gave them an opportunity for an 'upfront agenda setting' that allowed both parties to agree to address the most important issues within the time constraints.

The PCI-HN training hosted by experts in the field during the study day incorporated example video consultations with model PCI-HN use, the opportunity to discuss tactics for its use and anecdotes of successful implementation. A mixture of didactic teaching, visual resources and informal seminars allowed those with different learning styles to benefit from the session. Formalisation of video resources into 10-minute consultation appointments and the opportunity to receive one-to-one real time feedback were areas trainees highlighted for possible improvement during the study day.

Whilst the PCI-HN was developed within Oral and Maxillofacial Surgery (OMFS), it is being adapted and developed for use in other specialities including Ear, Nose and Throat (ENT) and Oncology. To ensure maximum benefit to patient and clinicians, appropriate training in its use and guidance, from senior clinicians already using the toolkit, is invaluable.

CONCLUSION

In terms of improved holistic consultations for HNC patients, both the PCI-HN and the PCI-HN specific simulated training have clear merits. Not only does the training give trainees the ability to effectively use the PCI in practice but also it provides a broader view of the patient's perspective. In future, training days within further surgical specialities can be modelled from this event.

REFERENCES

1. Rogers SN, Heseltine N, Flexen J, et al. Structured review of papers reporting specific functions in patients with cancer of the head and neck: 2006–2013. Brit J Oral Maxillofac Surg 2016; 54: e45–51.
2. Rogers SN, Miller RD, Ali K, et al. Patients' perceived health status following primary surgery for oral and oropharyngeal cancer. Int J Oral Maxillofac Surg 2006; 35: 913–9.
3. Rogers S, Semple C, Babb M, et al. Quality of life considerations in head and neck cancer: United Kingdom National Multidisciplinary Guidelines. J Laryngol Otol 2016; 130: S49–S52.
4. Lee EW, Twinn S, Moore AP, et al. Clinical encounter experiences of patients with nasopharyngeal carcinoma. Integr Cancer Ther 2008; 7: 24–32.
5. Mohd Shariff N, Azman N, Hami R, et al. Multicentre prospective cohort study of unmet supportive care needs among patients with breast cancer throughout their cancer treatment trajectory in Penang: a PenBCNeeds Study protocol. BMJ Open 2021; 11: e044746.
6. Surgeons RCo. Good Surgical Practice. A Guide to Good Practice. 2014.
7. Kanatas A, Lowe D, Rogers SN. The Patient Concerns Inventory in head and neck oncology: a structured review of its development, validation and clinical implications. Eur Arch Otorhinolaryngol 2022; 279(11): 5097–111.
8. Rogers SN, El-Sheikha J and Lowe D. The development of a Patients Concerns Inventory (PCI) to help reveal patients concerns in the head and neck clinic. Oral Oncol 2009; 45: 555–61.
9. Rogers SN, Allmark C, Bekiroglu F, Edwards RT, Fabbroni G, Flavel R, Highet V, Ho MWS, Humphris GM, Jones TM, Khattak O, Lancaster J, Loh C, Lowe D, Lowies C, Macareavy D, Moor J, Ong TK, Prasai A, Roland N, Semple C, Spencer LH, Tandon S, Thomas SJ, Schache A, Shaw RJ, Kanatas A. Improving quality of life through the routine use of the patient concerns inventory for head and neck cancer patients: main results of a cluster preference randomised controlled trial. Eur Arch Otorhinolaryngol 2021; 278(9): 3435–49.
10. Ezeofor V, Spencer L, Rogers S, et al. An Economic Evaluation Supported by Qualitative Data About the Patient Concerns Inventory (PCI) versus Standard Treatment Pathway in the Management of Patients with Head and Neck Cancer. PharmacoEconomics – Open 2022.
11. Rogers SN, Semple C, Humphris GM, Lowe D, Kanatas A. Using a patient prompt list to raise concerns in oncology clinics does not necessarily lead to longer consultations. Br J Oral Maxillofac Surg 2020; 58(9): 1164–71.
12. Teal CR, Street RL. Critical elements of culturally competent communication in the medical encounter: a review and model. Soc Sci Med 2009; 68(3): 533–43.
13. McMillan SS, Kendall E, Sav A, King MA, Whitty JA, Kelly F, Wheeler AJ. Patient-centered approaches to health care: a systematic review of randomized controlled trials. Med Care Res Rev 2013; 70(6):567–96.
14. Addeo R, Pompella L, Vitale P, et al. The Art of Counseling in the Treatment of Head and Neck Cancer: Exploratory Investigation among Perceptions of Health Professionals in Southern Italy. Curr Oncol 2022; 29: 6277–86.

15. Niglio de Figueiredo M, Krippeit L, Freund J, et al. Assessing Communication Skills in Real Medical Encounters in Oncology: Development and Validation of the ComOn-Coaching Rating Scales. J Cancer Educ 2019; 34: 73–81.
16. Tate P, Frame F. The doctor's communication handbook. CRC Press; 2019
17. Brooks J, McCluskey S, Turley E, King N. The utility of template analysis in qualitative psychology research. Qual Res Psychol 2015; 12(2): 202–22.
18. Nakagawa S, Fischkoff K, Berlin A, et al. Communication Skills Training for General Surgery Residents. J Surg Educ 2019; 76: 1223–30.
19. Low C, Fullarton M, Parkinson E, et al. Issues of intimacy and sexual dysfunction following major head and neck cancer treatment. Oral Oncol 2009; 45: 898–903.
20. Hoole J, Mitchell DA, Smith AB, et al. Mitchell–Hoole–Kanatas (MHK) questionnaire: the first to measure patient-reported outcomes relating to problems with intimacy after diagnosis and treatment of head and neck cancer. Br J Oral Maxillofac Surg 2018; 56: 910–7.
21. Duffy FD, Gordon GH, Whelan G, Cole-Kelly K, Frankel R, Buffone N, et al. Assessing competence in communication and interpersonal skills: the Kalamazoo II report. Acad Med 2004; 79(6): 495–507.
22. Elley CR, Clinick T, Wong C, Arroll B, Kennelly J, Doerr H, Moir F, Fishman T, Moyes SA, Kerse N. Effectiveness of simulated clinical teaching in general practice: randomised controlled trial. J Prim Health Care 2012; 4(4): 281–7.
23. Hardavella G, Aamli-Gaagnat A, Frille A, Saad N, Niculescu A, Powell P. Top tips to deal with challenging situations: doctor-patient interactions. Breathe (Sheff) 2017; 13(2): 129–35.

APPENDIX – SCENARIOS USED

SCENARIO A

48-year-old, female, operating theatre nurse assistant, working in the hospital and mother of three kids from 8–14 years old.

Past medical history:
– Asymptomatic multiple sclerosis.
– 2 years post-treatment for right maxillary sinus adenoid cystic carcinoma. This was excised with positive nerve margins and had radiotherapy. Following that she had wound breakdown and had 3 operations for reconstruction including a free flap. Following that she had right eye enucleation following poor healing and eye problems. She now wears a prosthesis.

In the clinic for her 3 monthly reviews, for cancer surveillance.
She is very concerned about cancer coming back, especially since she has an area of fluid discharge under the eye prosthesis. Recently her husband and family noticed her low mood and they feel she is depressed.
She is very worried about financial issues (especially since her kids are getting older).
She is still very angry that she was misdiagnosed by her GP and that delayed her treatment.

SCENARIO B

53-year-old male, leaves with partner, worked as a bank manager in full-time work.

Past medical history:
– 8 months post-surgical treatment for maxillary squamous cell carcinoma. Had a low-level maxillectomy and an obturator.

In clinic for his monthly cancer surveillance appointment.
He is very worried about his weight. He is unable to eat-his poor-fitting obturator is painful.
Also, when he is at work, drinks will come out of his nose. His voice is different, and this is very embarrassing for him. He had to leave from his workplace last week because he could not face his clients.
He wants to know if he had the right treatment and if his problems with the obturator can be solved in the clinic.

The specialist nurse mentioned that he told her he is struggling to sleep.

SCENARIO C

62-year-old retired engineer, married with 3 adult children. Lives with his wife.

Past medical history:
– Diabetic-well controlled.
– Hypertension on regular medication.

2 months ago – had extensive mandibular resection and reconstruction with fibula free flap and immediate implants.
This is his first clinic appointment after hospital discharge.

Problems:
His teeth feel different – as his 'bite' has changed.
Worried that his new bone has moved from the initial position – He 'knows' that for sure as he used to be an engineer.
Also, his left leg (donor site for fibula) – feels heavy. There is bleeding/smell/ discharge on his leg dressing – His community nurse told him that he has a leg infection.
He liked to go for a walk but he feels very tired now.
He wants to know when he will have his 'teeth' back – upset as he seems to be waiting for a long time.

SCENARIO D

66-year-old male. Retired long-distance driver, married and lives with his wife.

Past medical history:
– Haemophilia.

4 years ago, he had floor of mouth cancer treated with bilateral neck dissection, reconstruction with free flap and post-operative radiotherapy.
He has extensive osteoradionecrosis and had several debridement operations.
In clinic for his 4 monthly cancer surveillance appointment.

Problems:

Hole on his neck with communication with his mouth. Pain that needs regular morphine. Unable to eat solid food. Heard a noise and his jaw seems to be moving. Jaw shifted to the left. Food and saliva are coming through his neck.

He is angry that the cancer treatment destroyed his quality of life. He is unable to eat out. Does not enjoy his food and he is unable to swallow. He feels that life is not worth living now. Worried that his wife cannot cope with him, and he is concerned about his marriage. He feels that he cannot be intimate with his wife anymore, but he is embarrassed to discuss it.

SCENARIO E

32-year-old male, University lecturer, leaves with his male partner for the last 8 years.

Past medical history:
– Right tongue cancer was treated 9 months ago with surgery, neck dissection, free flap reconstruction from his left thigh and post-operative chemoradiotherapy.

In the clinic for his monthly cancer surveillance appointment.

Problems/concerns:

Still unable to eat, can only manage small pieces of solid food. Does not feel ready to go back to his university work. He is worried about his speech. He is very worried that he will not be able to lecture again and that he will not be able to go back to work. With his partner, they bought a house and worried about the mortgage payments.

He read that HPV cause cancer and wants to be tested for that. He is worried that his male partner may get cancer too.

He loved swimming but his shoulder stiffness is a problem. Wants to know what can be done.

He is not a smoker or drinker and wants to know why he had cancer. Worried that the cancer will come back.

SCENARIO F

42-year-old lawyer and mother of two young daughters. Currently off work.

Past medical treatment:
– Kidney transplant when she was 36 on immunosuppression (tacrolimus).
– 9 months post-treatment for gingival cancer. She had surgery with teeth extractions, neck dissection and postoperative radiotherapy to her neck.

In the clinic for her monthly cancer surveillance appointment.

Problems/concerns:

The neck scar feels tight and painful during the cold weather. Likes to cover it. Does not like the look of it – it reminds her of 'the cancer'.

Had clinical psychology input but worried that she will not see her daughter going to university. Has 'no-one' to talk to about that and her family does not seem to help her.

Worried that it was the spicy food (as she is of Indian origin) that caused her cancer.

She wants to know if she can have 'gene testing' – she read that cancer is hereditary and wants to 'prevent' her kids from getting cancer.

Self-reported Side Effects of SARS-CoV-2 Vaccination

Josef Finsterer[1],*, Danice Hertz[2]

ABSTRACT

SARS-CoV-2 vaccines are often promoted as safe. However, real world data tell a different story. The aim of this study is to investigate the type and frequency of adverse reactions to SARS-CoV-2 vaccination in a randomly selected cohort of unrelated individuals. Adverse reactions to the first/second dose of a SARS-CoV-2 vaccine were recorded using an online reporting system called "Pabbly". Patients were asked via social media to report any symptoms temporarily associated with vaccination. One hundred subjects were enrolled. The mean age was 42.6 years (range: 12–74 years). Ninety-one percent were female. The latency period between vaccination and onset of symptoms ranged from zero to 18 days. The most commonly reported symptoms were tingling/vibration/tremor (79%), numbness (57%), heart problems (53%), muscle weakness/muscle pain (45%), dizziness (44%), headache (44%) and fatigue (43%). Three patients developed small fiber neuropathy. Three patients had COVID-19 prior to vaccination. Of the included subjects, 37% had to be hospitalized. Overall, SARS-CoV-2 vaccination is not without side effects, regardless of the product used. In most cases, the reported side effects were not life-threatening, but one third of study participants experienced serious side effects requiring hospitalization and intensive care. Manufacturers of SARS-CoV-2 vaccines should respond appropriately to reports of adverse reactions associated with SARS-CoV-2 vaccination.

AUTHOR AFFILIATIONS

[1] Neurology & Neurophysiology Center, Vienna, Austria
[2] Private office, Santa Monica, CA, USA
* Postfach 20, 1180 Vienna, Austria; e-mail: fifigs1@yahoo.de

INTRODUCTION

Vaccination with SARS-CoV-2 vaccines is generally well tolerated, but in some cases mild or severe adverse reactions may occur (1). These side effects may occur within a few days after vaccination (acute COVID-19 vaccination syndrome (ACVS)) or weeks or months after vaccination (post-acute COVID-19 vaccination syndrome (PACVS)) (2). Although health care workers in most health care systems are required to report such side effects to health authorities, publishing side effects of SARS-CoV-2 vaccinations is contrary to political intentions in many countries. This is because politicians are called upon to overcome the pandemic, and the most widespread strategies implemented are vaccination, testing, social distancing and lockdowns. Since vaccination is promoted to be the best way to control the pandemic, there is an urgent need to have an effective and safe weapon at hand. However, real-world data increasingly suggest that adverse reactions to SARS-CoV-2 vaccination are occurring, which may be a reason why the targeted vaccination rates are not being achieved in many countries. The following cohort study was conducted to investigate in a real-world setting which symptoms occur in vaccinated subjects in temporal relation to vaccination.

METHODS

The data was collected as part of an online survey called "Pabbly". "Pabbly" was created by one of the co-authors who had technical computer skills. The subjects were actively asked via social media to report their side effects of the vaccination to Pabbly. These patients were members of private Facebook groups for those affected by vaccination. The information collected was then retrieved and placed into a spreadsheet format to make it easier to interpret and extract better personal health information. All subjects who provided their individual epidemiological data and completed the questionnaire correctly were included. Patients who provided incomplete or inconclusive individual information were excluded. It was not recorded whether these symptoms resolved spontaneously, persisted, or required therapeutic intervention with partial or complete resolution. The study adhered to the tenets of the Declaration of Helsinki.

RESULTS

A total of 100 participants completed the online survey. Ninety-one percent of the participants were female. The average age of the 97 participants who reported their age, was 42.6 years (range: 12–73 years). In terms of race/ethnicity, 88% were white, 5% Hispanic, 3% African American, 2% Asian, and 1% each Pacific Islander and Alaskan Native respectively (Figure 1). Of the 100 participants, 49% received the Moderna vaccine, 43% received the Pfizer vaccine, 5% received the J&J vaccine, and 3% received the AstraZeneca vaccine (Figure 2). The latency period between vaccination and onset of symptoms ranged from zero to 18 days. In 86% of cases, side effects occurred within the

first 7 days after the vaccination. Side effects occurred in 74 patients after the first dose and in 26 patients after the second dose. The most commonly reported symptoms included tingling/vibrations/shaking feeling in 79%, numbness in 57%, heart issues in 53%, muscle weakness/muscle pain in 45%, dizziness in 44%, headache in 44%, generalized fatigue in 43%, stomach discomfort in 42%, brain fog in 39%, involuntary twitching in 36%, limb tremor in 29%, blood pressure abnormalities in 27% and tinnitus in 20% of the cases (Figure 3). In addition to these symptoms, other less commonly reported complaints have been noted, including visual disturbances, insomnia, temperature regulation issues, lymphadenopathy, menstrual irregularities, arthralgias, hypersensitivity to light and sound, skin rashes and burning sensations. Small fibre neuropathy was reported in 3 patients. Most patients had a unique set of symptoms. Of the 100 participants, 37% required hospitalization due to the severity of their complaints. However, some patients with serious side effects were not hospitalised because they were not taken seriously or because hospital capacity was reduced. Three percent of the cohort had COVID-19 prior to vaccination. Fourteen patients received the second dose despite experiencing side effects after the first dose.

DISCUSSION

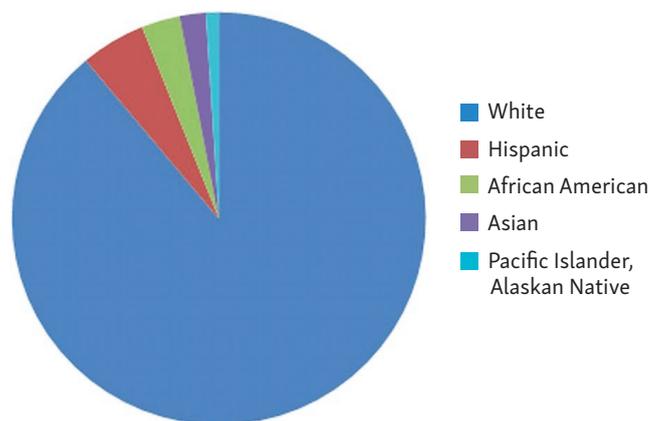The study shows that each of the licensed SARS-CoV-2 vaccines can be associated with adverse reactions. In the

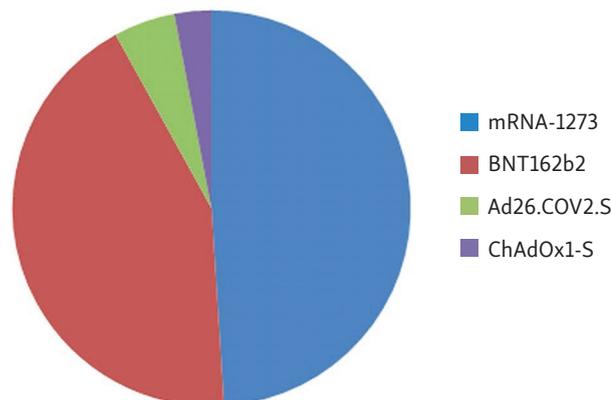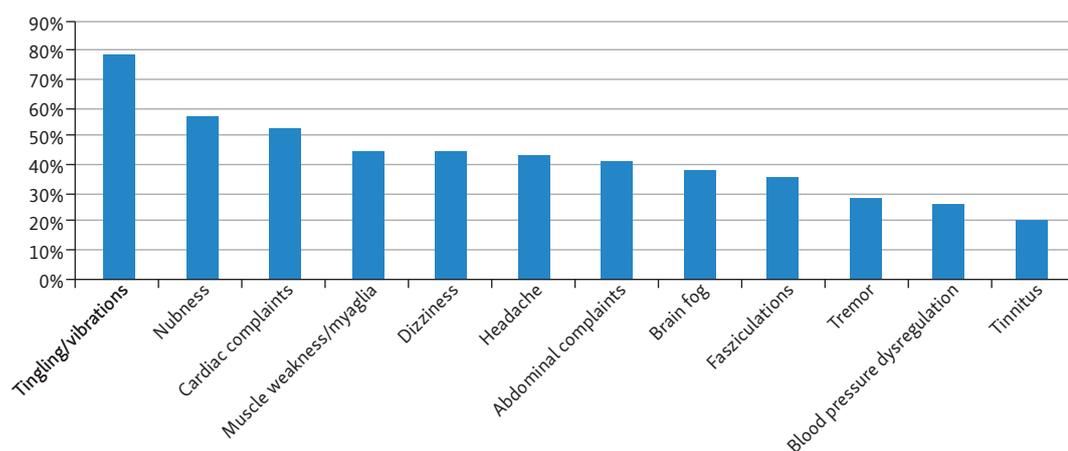**Fig. 1** Ethnic distribution of the included patients in percent.

Fig. 2 Frequency of vaccine brands used in the study.

Fig. 3 Frequency of the most common side effects reported by the 100 included patients.

majority of these cases, the adverse reactions were not life-threatening, but in isolated cases serious side effects were observed, requiring hospitalization in about one third of the subjects. In view of these results, individuals should be informed about possible side effects before vaccination and, if they occur, patients should be taken seriously, and the side effects carefully reported and analyzed.

There is increasing evidence from non-industry-supported studies that SARS-CoV-2 vaccinations are not free of side effects and that all available, commercial brands can be complicated by ACVS or PACVS in previously healthy subjects, but even more so in subjects with pre-existing illnesses (3–5). In general, side effects of SARS-CoV-2 vaccination may be specific or non-specific. Specific side effects may manifest themselves in the central and peripheral nervous system (CNS/PNS), heart, intestines, blood coagulation system, lymphatic system, bone marrow, or skin. According to published data, the most common CNS complications to SARS-CoV-2 vaccination include sinus venous thrombosis, headache (6–7), acute disseminated encephalomyelitis (ADEM) (8), acute encephalitis (9), and transverse myelitis (10). PNS complications following SARS-CoV-2 vaccinations include Guillain-Barre syndrome (GBS) (11). Cardiac complications of SARS-CoV-2 vaccinations include acute myocardial damage, myocarditis or perimyocarditis (12, 13). Gastro-intestinal side effects of SARS-CoV-2 vaccination include autoimmune hepatitis, nausea, and vomiting (7). There is a report of a fatal pulmonary embolism one day after the first dose of the AstraZeneca vaccine. The lymphatic system can react with lymphadenopathy (7, 14). Bone marrow problems can manifest as hemolytic anemia (10) or immune thrombocytopenia. Dermatological manifestations following SARS-CoV-2 vaccination include bullous rash (15), erythema (7), zoster, angioedema, wheals, scaly plaques, erythematous patches, and macules and papules (16, 17). Non-specific side effects include fever, fatigue, arthralgia, swelling, chills, warmth, myalgia and local injection site reactions including induration, tenderness and itching (7, 18, 19). These previously reported nonspecific side effects are consistent with those reported in the present study. In a single-blind, randomised, controlled, phase 2/3 trial of 160 participants receiving the AstraZeneca vaccine, fatigue,

headache, myalgia, and malaise were the most common side effects, but these manifestations were age-dependent (18). In a post-marketing study of 3732 participants who received the Moderna vaccine, the most common side effects reported after the first/second dose were injection site pain (93.1/92.4%), headache (44.6/70.2%), and fatigue (47.9/67.8%) (20).

The predominance of Moderna in the present study could be explained by the availability of this vaccine in the areas where an adverse reaction was reported. However, the availability of vaccines was not recorded for this study. The preponderance of women may be explained by a presumed greater interest among women in reporting their complaints. Women may also have stronger autoimmune tendencies. There is limited data on how often patients with side effects from SARS-CoV-2 vaccination require treatment, what treatment is used, and how many of those treated benefit. At present, there are currently very limited treatment options available for these adverse reactions. According to available data, a third of patients required hospitalization, which could place an additional burden on healthcare systems. There is therefore a need to develop new vaccines with fewer side effects and better tolerability.

The main limitation of the study is the small number of patients enrolled. The second limitation is that the enrolment procedures relied on selection bias. A third limitation is that no control group was included. Further limitations of the study are that no data were collected for medical clarification of the symptoms and the duration between onset and follow-up care was not documented. It remains unknown how many of the subjects reported their post-vaccination complaints to the "Vaccination Adverse Event Reporting System" (VAERS).

In conclusion, SARS-CoV-2 vaccination is not without side effects, regardless of the product used. In the case of this study, most side effects were not life-threatening, but one third of the subjects with complaints experienced serious adverse reactions that required hospitalization and intensive care treatment. Physicians should be aware that COVID-19 vaccination carries the risk of ACVS and PACVS and should take patients' post-vaccination complaints seriously. These reactions should be thoroughly documented

and reported to the appropriate health authorities, including VAERS, as well as to the vaccine manufacturers. Manufacturers of SARS-CoV-2 vaccines are urged to take side effects seriously and be cautious when promoting their current products for all age groups or for multiple booster vaccinations.

FUNDING

No funding was received.

CONFLICTS OF INTEREST

None

ETHICS APPROVAL

Only secondary data were used.

AVAILABILITY OF DATA

All data are available from the corresponding author.

AUTHOR CONTRIBUTION

JF: design, literature search, discussion, first draft, critical comments, final approval, DH: literature search, discussion, critical comments, final approval.

REFERENCES

1. Finsterer J. Neurological Adverse Reactions to SARS-CoV-2 Vaccines. Clin Psychopharmacol Neurosci 2023; 21(2): 222–39.
2. Scholkmann F, May CA. COVID-19, post-acute COVID-19 syndrome (PACS, "long COVID") and post-COVID-19 vaccination syndrome (PCVS, "post-COVIDvac-syndrome"): Similarities and differences. Pathol Res Pract 2023; 246: 154497.
3. Eterafi M, Fouladi N, Golizadeh M, Shaker H, Matin S, Safarzadeh E. Reported side-effects following Oxford/AstraZeneca COVID-19 vaccine in the north-west province, Iran: A cross-sectional study. PLoS One 2024; 19(1): e0296669.
4. Melanson SEF, Zhao Z, Kumanovics A, Love T, Meng QH, Wu AHB, Apple F, Ondracek CR, Schulz KM, Wiencek JR, Koch D, Christenson R, Zhang YV. Tolerance for three commonly administered COVID-19 vaccines by healthcare professionals. Front Public Health 2022; 10: 975781.
5. Schmidt M, Hébert S, Wallukat G, Ponader R, Krickau T, Galiano M, Reutter H, Woelfle J, Agaimy A, Mardin C, Hoerning A, Hohberger B. "Multisystem Inflammatory Syndrome in Children" – Like Disease after COVID-19 Vaccination (MIS-V) with Potential Significance of Functional Active Autoantibodies Targeting G-Protein-Coupled Receptors (GPCR-fAAb) for Pathophysiology and Therapy. Children (Basel) 2023; 10(12): 1836.
6. Göbel CH, Heinze A, Karstedt S, et al. Headache Attributed to Vaccination Against COVID-19 (Coronavirus SARS-CoV-2) with the ChAdOx1 nCoV-19 (AZD1222) Vaccine: A Multicenter Observational Cohort Study. Pain Ther 2021: 1–22.
7. Vogrig A, Janes F, Gigli GL, et al. Acute disseminated encephalomyelitis after SARS-CoV-2 vaccination. Clin Neurol Neurosurg 2021; 208: 106839.
8. Sarmast ST, Mohamed AS, Amar Z, Sarwar S, Ahmed Z. A Case of Acute Encephalitis in COVID-19 Patient: A Rare Complication. Cureus 2021;13: e15636.
9. Hasnie AA, Hasnie UA, Patel N, et al. Perimyocarditis following first dose of the mRNA-1273 SARS-CoV-2 (Moderna) vaccine in a healthy young male: a case report. BMC Cardiovasc Disord 2021; 21: 375.
10. Voysey M, Clemens SAC, Madhi SA, et al. Oxford COVID Vaccine Trial Group. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet 2021; 397(10269): 99–111.
11. Finsterer J. Guillain-Barre syndrome 15 days after COVID-19 despite SARS-CoV-2 vaccination. IDCases 2021; 25: e01226.
12. Williams CB, Choi JI, Hosseini F, Roberts J, Ramanathan K, Ong K. Acute Myocarditis Following mRNA-1273 SARS-CoV-2 Vaccination. CJC Open 2021; 3(/11): 1410–12.
13. McIntosh LJ, Rosen MP, Mittal K, et al. Coordination and optimization of FDG PET/CT and COVID-19 vaccination; Lessons learned in the early stages of mass vaccination. Cancer Treat Rev 2021; 98: 102220.
14. Kong J, Cuevas-Castillo F, Nassar M, et al. Bullous drug eruption after second dose of mRNA-1273 (Moderna) COVID-19 vaccine: Case report. J Infect Public Health 2021; 14(10): 1392–4.
15. Baden LR, El Sahly HM, Essink B, et al. COVE Study Group. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med 2021; 384: 403–16.
16. Akdaş E, Öğüt B, Erdem Ö, Öztaş MO, İlter N. Cutaneous reactions following CoronaVac COVID-19 vaccination: a case series of six healthcare workers from a single center. J Eur Acad Dermatol Venereol 2021; 35(12): e861–e864.
17. Mouliou DS, Dardiotis E. Current Evidence in SARS-CoV-2 mRNA Vaccines and Post-Vaccination Adverse Reports: Knowns and Unknowns. Diagnostics (Basel) 2022; 12(7): 1555.
18. Ramasamy MN, Minassian AM, Ewer KJ, et al. Oxford COVID Vaccine Trial Group. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. Lancet 2021; 396(10267): 1979–93.
19. Folegatti PM, Ewer KJ, Aley PK, et al. Oxford COVID Vaccine Trial Group. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. Lancet 2020; 396(10249): 467–78.
20. Ali K, Berman G, Zhou H, et al. Evaluation of mRNA-1273SARS-CoV-2 Vaccine in Adolescents. N Engl J Med 2021; 385(24): 2241–51.

Commonly Misdiagnosed Facial Lesion: Pilomatricoma

Tan Ying Xin[1], Jeyasakthy Saniasiaya[1,*], Jeyanthi Kulasegarah[1], Chiew Seow Fan[2]

ABSTRACT

Pilomatricoma, also known as Pilamatrixoma or Malherbe's calcifying epithelioma, is a benign skin tumour with a bimodal age distribution between the paediatric and elderly age groups. Although it was previously thought to be rare, recent studies have revealed that it is quite common. Typically, pilomatricoma is diagnosed following histopathological examination of the lesion as it is frequently misdiagnosed with other types of skin pathology. In our case, the child presented with painless swelling of the left infraauricular region. The initial cytology and imaging were unable to provide a definite diagnosis. An excision biopsy was done, and a histopathological examination was suggestive of Pilomatricoma. Therefore, Pilomatricoma ought to be considered in the differential diagnosis of head and neck lesions in hopes of providing a better understanding on this pathological lesion.

AUTHOR AFFILIATIONS

[1] Department of Otorhinolaryngology, Faculty of Medicine, University of Malaya, Jalan Universiti, 50603 Kuala Lumpur, WP Kuala Lumpur, Malaysia
[2] Department of Pathology, Faculty of Medicine, University of Malaya, Jalan Universiti, 50603 Kuala Lumpur, WP Kuala Lumpur, Malaysia
* Corresponding author: Department of Otorhinolaryngology, Faculty of Medicine, University of Malaya, Jalan University, 50603 Kuala Lumpur, WP Kuala Lumpur, Malaysia; e-mail: shakthy_18@yahoo.com

INTRODUCTION

Malherbe and Chenantais, in 1880 described a benign skin lesion which was called the calcifying epithelioma (1). Forbis and Helwig later discovered through histopathological examination that the lesion originated from the matrix cells of hair follicles (2, 3). Since then, this benign lesion was referred to as "Pilomatricoma" or "Pilomatrixoma", which typically manifest in the first or second decade of life. A slight predominance of females was reported. Most of this entity manifested as a single slow-growing, painless, firm mobile lesion. Due to its origin, it adhered to the skin but not the underlying tissue. It is commonly found in the head, neck, and upper extremities, particularly on the face (4) and was typically small, measuring less than 5 cm. Although not uncommon, it was frequently misdiagnosed as other facial lesions such as sebaceous cysts, dermoid cysts, foreign body reaction, calcified lymph nodes, fat necrosis and cartilage (1, 4). It was diagnosed post-operatively by identifying islands of epithelial cells containing basophilic cells, ghost cells, and, on rare occasions, foreign body giant cells and calcifications during histopathological examination (5). The only treatment is surgical resection. It rarely recurs or progresses to cancer. This case report aims to raise awareness of this tumor so that it is not overlooked in the differential diagnosis.

CASE REPORT

A previously healthy 11-year-old boy presented with a two-week history of left infraauricular swelling. He was otherwise well. No other ear, nose or throat symptoms were reported. There were no constitutional or B symptoms (this is the full name. It's a triad of symptoms namely fever, night sweat and significant weight loss which may suggest of lymphoma). No recent sick contact or similar episode in the family. The child's immunization record was up to date, and his developmental milestone was according to age.

On examination, a 1 × 1 cm firm, non-tender, mobile, painless swelling was found in the left infrauricular region. There were no overlying skin changes or palpable neck nodes. Other examinations were normal. He was treated as an infected sebaceous cyst and was given a course of oral antibiotics. However, he defaulted the follow-up due to logistic issue. He returned to us seven months later due to persistent swelling. The lesion remained the same size with no signs of inflammation or infection. Blood infective parameters and tuberculosis screening were within normal parameters.

Ultrasonography demonstrated a well-defined heterogeneous solid lesion in the subcutaneous area of the left infraauricular region measuring 0.7 × 1.3 cm (Fig. 1). Fine needle aspiration (FNAC) of the lesion revealed acellular squames.

The child then underwent excision of the left infraauricular mass. Intraoperatively the lesion was superficial, measuring 1.0 × 1.0 cm, and located beneath the subcutaneous tissue (Fig. 2). The histopathological examination of the lesion showed features suggestive of pilomatricoma. Fig. 3 showed aggregates of foreign body type multinucleated giant cells intermixed with anucleated shadow cells.

Fig. 2 Histopathological examination of the lesion showing aggregates of foreign body type multinucleated giant cells intermixed with anucleated shadow cells.
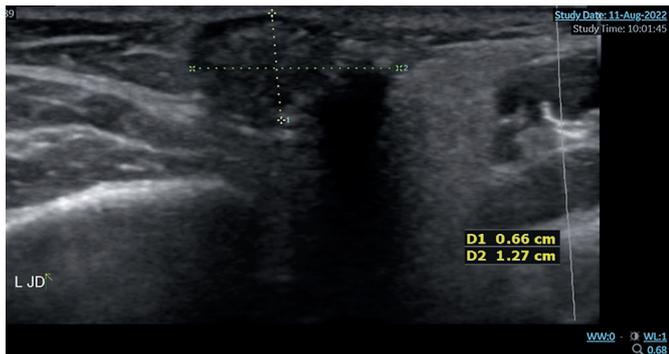
Fig. 1 Ultrasonography of a well-defined heterogeneous solid lesion measuring 0.7 × 1.3 cm.
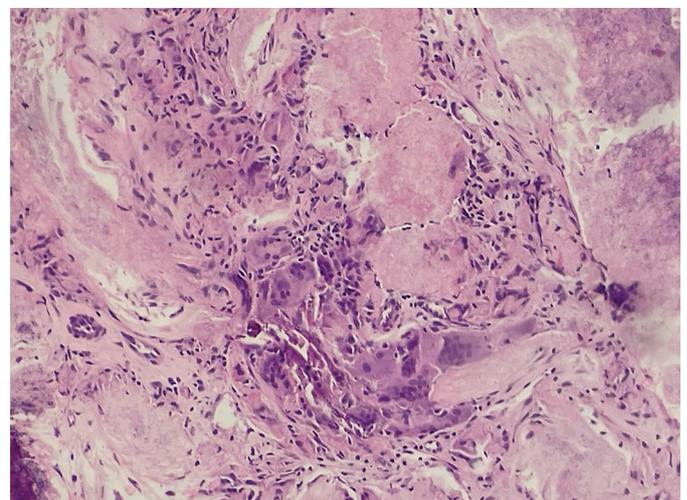
Fig. 3 Nodules of anucleated shadow cells and calcification, with cholesterol cleft.

DISCUSSION

The majority of Pilomatricoma studies revealed bimodal age distribution. It usually peaked in the first two decades or between the ages of 40 to 60 (4, 6). It is commonly found in children. 40% occur before the age of ten, and 20% occur between the age of eleven to twenty (7). It is slightly more common in female (7, 8). The common locations of Pilomatricoma were the head and neck, upper extremities, trunk, and lower extremities (2–4). In addition to that, 40% of them were discovered on the head, particularly in the cheek or palpebral area (4, 7). Nonetheless, despite its frequency, preoperative diagnosis was only achieved in approximately 28.9 to 43 percent of cases due to non-specific presentation and imaging (4).

The most common presentation of Pilomatricoma was solitary, firm, painless swelling, as noted in our case. The lesion commonly located in the deep dermis or subcutaneous layer (3, 4). This gave them the characteristic of skin adherence but mobile from the below structure (1). Due to the presence of blood vessels in the lesion, some will have bluish-red discoloration (7). "Tent sign" was a unique feature of Pilomatricoma. It was caused by tumoral calcification in the skin caused by excessive tension, resulting in tense skin with multiple facets and angles (3, 4). Although the lesion was usually solitary, it can present as multiple nodules in 2-9 percent of cases (4). Multiple lesions were common in people with genetic diseases (8). The genetic disease that was commonly associated with pilomatricoma were Gardner syndrome, myotonic dystrophy and Turner Synrdome (7). Turner Syndrome and myotonic dystrophy account for 42% of genetic diseases associated with Pilomatricoma (7).

Ultrasonography is the most commonly used method because it is non-invasive, non-radiative, inexpensive, and quick, making it ideal for use in children. In ultrasound, the lesion appeared as well-defined, ovoid, hypoechoic, heterogenous masses with or without posterior shadowing (7). In our case, an ultrasound revealed a well-defined heterogeneous solid lesion measuring 0.7 × 1.3 cm in the subcutaneous area of the infraauricular region. Computed tomography is another imaging option for Pilomatricoma, although it is non-specific (9), with well-defined subcutaneous mass seen with mild to moderate enhancement with calcifications.

The classical cytological triad features of Pilomatricoma include basaloid cells, ghost cells and giant cells, albeit present in only 40% of cytology (7). Moreover, only 44% of the lesions can be correctly diagnosed using FNAC (7) which results in a diagnostic dilemma. In our case, FNAC revealed acellular squames, whereas histopathological examination revealed a triad of basaloid epithelium, ghost cell, and giant cell, indicating Pilomatricoma.

Differential diagnosis for Pilomatricoma include sebaceous cysts, dermoid cysts, foreign body reaction, calcified lymph nodes, fat necrosis and cartilage (1, 4). The majority of them are difficult to distinguish based on history and clinical examination, and will require a histopathological examination.

It is worth noting that, Pilomatricoma does not regress on its own and cannot be treated using pharmacological treatment (6). The primary treatment for it is complete surgical resection. Because the preoperative diagnosis is usually speculative, surgical resection is typically deemed for diagnostic confirmation. Additionally, a low recurrence rate of 0–3% (6) had been documented, usually caused by incomplete resection (7). Recurrence in this entity occur between a year and a decade after resection (4). In view of the low recurrence rate, long-term follow-up is not required. Yet, malignancy must be ruled out in patients suspected of Pilomatricoma recurrence, albeit rare and involving the elderly age group (4). So far, only one case of malignant transformation in children with Pilomatricoma has been reported (4). In the same vein, a safe surgical margin of 1–2 cm is required for the excision of pilomatricoma carcinoma as it has been reported to metastasize. Hence, long-term follow-up is warranted post-resection.

CONCLUSION

Pilomatricoma is a relatively common benign skin tumour in children, which is frequently overlooked. However, by increasing the awareness, more research can be carried out to better understand this entity.

REFERENCES

1. Kumaran N, Azmy A, Carachi R, Raine PA, Macfarlane JH, Howatson AG. Pilomatrixoma-accuracy of clinical diagnosis. J Pediatr Surg 2006; 41(10): 1755–8.
2. Missak M, Haig A, Gabril M. Pilomatrixoma with Atypical Features: A Case Report. Case Rep Dermatol 2021; 13: 98–102.
3. Kose D, Ciftci I, Harmankaya I, Ugras S, Caliskan U, Koksal Y. Pilomatrixoma in childhood. J Can Res Ther 2014; 10: 549–51.
4. Hu JL, YooH, Kwon ST, et al. Clinical analysis and review of literature on pilomatrixoma in pediatric patients. Arch Carniofac Surg 2020; 21(5): 288–93.
5. Agarwal RP, Handler SD, Matthews MR, Carpentieri D. Pilomatrixoma of the head and neck in children. Otolaryngol Head Neck Surg 2001; 125(5): 51–5.
6. Nadershah M, Alshadwi A, Salama A. Recurrent giant pilomatrixoma of the face: a case report and review of the literature. Case Rep Dent 2012; 2012: 197273.
7. Jones CD, Ho W, Robertson BF, Gunn E, Morley S. Pilomatrixoma: A Comprehensive Review of the Literature. Am J Dermatopathol 2018; 40(9): 631–41
8. Lan MY, Lan MC, Ho CY, Li WY, Lin CZ. Pilomatricoma of the head and neck: a retrospective review of 179 cases. Arch Otolaryngol Head Neck Surg 2003; 129(12): 1327–30.
9. Saniasiaya J, Mohamad I, Kamaludin Z. Pilomatrixoma of the neck: A forgotten entity. Egypt J Ear, Nose, Throat Allied Sci 2017; 18(3): 311–2.

Tortuosity and Pulsatility of the Tibial Artery – Two Case Reports of a Rare Etiology of Tarsal Tunnel Syndrome

Márcio Luís Duarte[1],*, Mayara Oliveira da Silva[2], Ocacir de Souza Reis Soares[3]

ABSTRACT

Tarsal tunnel syndrome is a neuropathic compression of the tibial nerve and its branches on the medial side of the ankle. It is a challenging diagnosis that constitutes symptoms arising from damage to the posterior tibial nerve or its branches as they proceed through the tarsal tunnel below the flexor retinaculum in the medial ankle, easily forgotten and underdiagnosed. Neural compression by vascular structures has been suggested as a possible etiology in some clinical conditions. Tibial artery tortuosity is not that rare, but only that it affects the nerve can cause tarsal tunnel syndrome. Therefore, a study care must be taken to avoid false-positive errors.

KEYWORDS

Nerve Compression Syndromes; Tarsal Tunnel Syndrome; Tibial nerve; ultrasonography; diagnosis

AUTHOR AFFILIATIONS

[1] Radiology professor at Universidade de Ribeirão Preto Campus Guarujá, Guarujá-SP, Brazil
[2] Biomedical at Universidade Federal de São Paul, Santos-SP, Brazil
[3] Radiologist at Clínica Radiológica Ocacir Soares, Presidente Prudente, São Paulo, Brazil
* Corresponding author: Universidade de Ribeirão Preto Campus Guarujá. Avenida Dom Pedro I, 3300 Guarujá-SP, Brazil.
  ZIP CODE: 11440-003; e-mail: marcioluisduarte@gmail.com

INTRODUCTION

The tibial nerve passes through the medial side of the ankle and branches into the medial plantar nerve, lateral plantar nerve and medial calcaneal branch (1). This area is called the tarsal tunnel and is composed of the posterior tibial tendon, long flexor tendon of the fingers, neurovascular bundle and flexor hallucis longus tendon (medial to lateral) (1, 2).Therefore, small changes in this space can easily result in neuropathy (2).

Tarsal tunnel syndrome (TTS) is a neuropathic compression of the tibial nerve and its branches on the medial side of the ankle and, although descriptions of TTS symptoms vary, most authors consider symptoms of acute pain, pain when standing in standing or walking for a long time, numbness, paresthesia or burning sensations involving the foot (1, 3). It occurs for various etiologies and the frequency of different etiologies varies in the literature and the cause of compression is detected in about 60–80% (2, 3). The causes of tarsal tunnel syndrome can be (3):

–   Bone disorders: talocrural and subtalar arthritis; arthropathy with synovitis and talocalcaneal synostosis; stalk support; fracture sequelae; change in static foot posture.
–   Tendon disorders: tendinopathy and flexor tenosynovitis.
– Vascular disorders: tibial artery tortuosity, venous aneurysms, and varicose plantar veins.
–   Idiopathic.
–   Expansive lesions: ganglion cysts, particularly epineural, soft tissue tumors, including intracanal lipoma, and tumors of neural origin.
–   Muscle
    •   Supernumerary muscles: accessory soleus muscle, medial fibulocalcaneus muscle and, mainly, accessory digital flexor muscle.
    •   Muscle hypertrophy: abductor hallucis muscle or flexor hallucis muscle.
–   Trauma: bone diseases, ligament injuries, flexor retinaculum thickening, hematoma, fibrosis and iatrogenic nerve damage

Tarsal tunnel syndrome is a challenging diagnosis that constitutes symptoms arising from damage to the posterior tibial nerve or its branches as they proceed through the tarsal tunnel below the flexor retinaculum in the medial ankle, easily forgotten and underdiagnosed (4). According to electrophysiological investigations, the prevalence of tarsal tunnel syndrome is registered 0.4–0.5% (5).

We demonstrate two cases of tarsal tunnel syndrome caused by tibial artery pulsatility and tortuosity, a situation first reported by Kim et al. (2) in 2010.

CASE REPORT 1

A 62-year-old woman reported pain, tingling and numbness in the medial region of the ankle for a year, with worsening for two months, worsening when walking or standing for a long time. She reports pain on palpation in
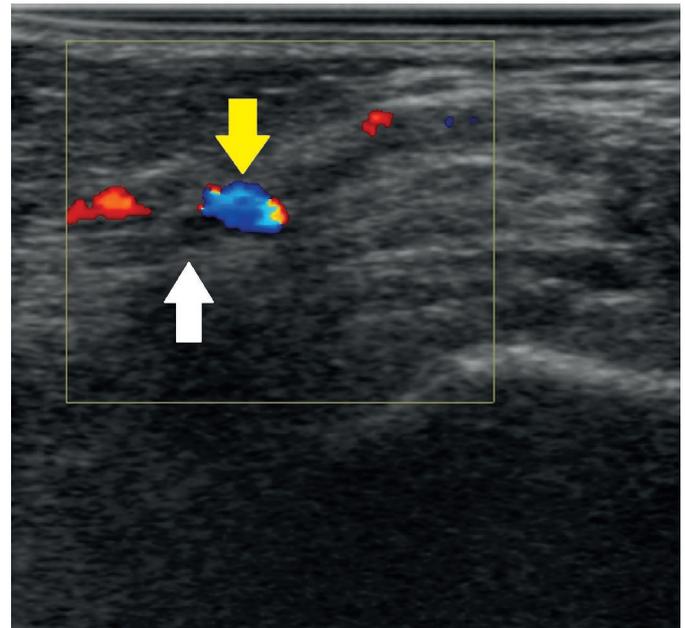
Fig. 1 Color Doppler ultrasound showing tibial artery tortuosity (yellow arrow) compressing the tibial nerve (white arrow) characterizing tarsal tunnel syndrome caused by tibial artery pulsatility and tortuosity.
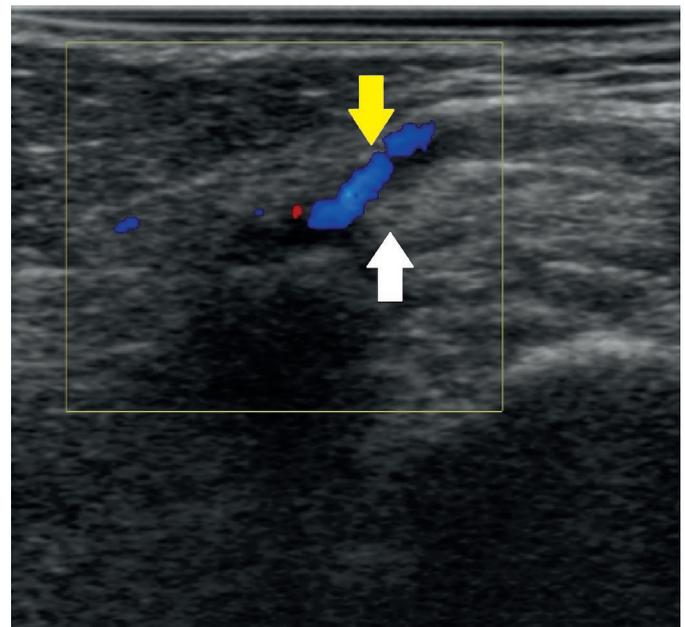
Fig. 2 Color Doppler ultrasound showing tibial artery tortuosity (yellow arrow) compressing the tibial nerve (white arrow) characterizing tarsal tunnel syndrome caused by tibial artery pulsatility and tortuosity.

the region, limiting the variety of shoes, using only sneakers. Denies diabetes mellitus. On physical examination, she has no limitation in movement of the joint, but has a positive Tinel's sign.

Ankle ultrasound detects the tortuous tibial artery in contact with the tibial nerve and compressing it according to its pulsation, characterizing tarsal tunnel syndrome caused by the pulsatility and tortuosity of the tibial artery (Video; Figures 1 and 2). The ultrasound also detects tibial

nerve thickening cross-sectional area of the tibial nerve was 0.20 cm².

She was treated with physiotherapy for four months reporting great improvement of numbness and pain (informs about 80%), but still having some episodes of tingling. She also reports wearing a variety of shoes that she was unable to use.

VIDEO

Video is available at: https://youtu.be/WxbyzIfzY4M. Color Doppler ultrasound showing tibial artery tortuosity compressing the tibial nerve characterizing tarsal tunnel syndrome caused by tibial artery pulsatility and tortuosity.

CASE REPORT 2

A 55-year-old woman reported pain, tingling and numbness in the ankle for two months. Refers worsening when standing for a long time and walking. Informs difficult in wearing shoes due to pain in the region. Denies diabetes mellitus. On physical examination, she has no limitation in movement of the joint, but has a positive Tinels sign.

Ankle ultrasound detected the tortuous tibial artery in contact with the tibial nerve and compressing it according to its pulsation. Also, is detected compression of the tibial nerve by varicose plantar veins. Both causes of compression characterizes causes of tarsal tunnel syndrome (Figures 3 and 4). The ultrasound detects tibial nerve thickening cross-sectional area of the tibial nerve was 0.20 cm². Doppler ultrasound of lower limbs confirmed the varicose plantar veins.

The patient started treatment muscle strengthening, physiotherapy and compression socks and after three weeks she has no symptoms. She also reports wearing shoes that she stopped to use.

DISCUSSION

Reliable diagnosis requires confirmation of focal pathology of the tibial nerve in the tarsal tunnel (6). Due to the superficial location of the tunnel, the resolution obtained with ultrasonography is considerably better than that obtained with magnetic resonance imaging (MRI) (6). When the syndrome of the tarsal tunnel is suspected, ultrasonography should be performed routinely (1, 3). Ultrasonography with the Tinel test should be performed by touching the nerve to induce symptoms, as if positive, it suggests the diagnosis of tarsal tunnel syndrome (3).

Neural compression by vascular structures has been suggested as a possible etiology in some clinical conditions (2). Tibial artery tortuosity is not that rare, but only that it affects the nerve it can cause tarsal tunnel syndrome (3). Therefore, a study care must be taken to avoid false-positive errors (7). As dynamic analysis is possible with ultrasonography, arterial pulsation is easily assessed (7). Nerve compression is worsened by plantar flexion, and it is attributable to the shift in the deformed angle of the
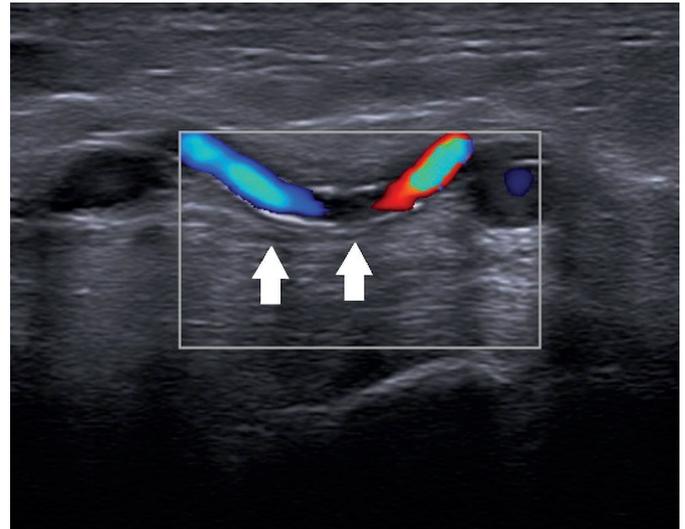
Fig. 3 Color Doppler ultrasound showing tibial artery tortuosity compressing the tibial nerve (white arrows) characterizing tarsal tunnel syndrome caused by tibial artery pulsatility and tortuosity.
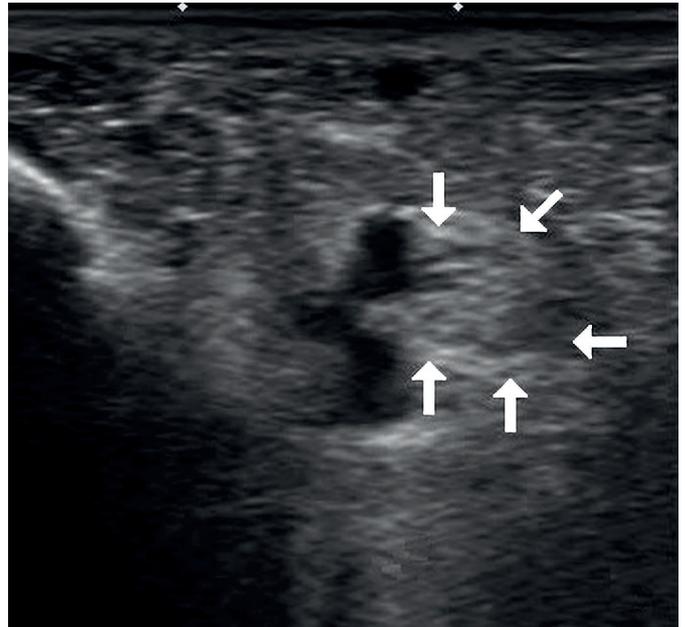
Fig. 4 Grayscale ultrasound showing varicose plantar veins compressing the tibial nerve (white arrows).

posterior tibial artery (8). This type of information is useful in determining the positional relationships of expansive lesions in the tarsal tunnel and the tibial nerve (1).

A burning sensation or numbness in the feet is a disorder frequently encountered by physicians (2). Patients often complain of sensory disturbances, localized or radiating pain, burning pain, paresthesia, and abnormal temperature perception (2). The most common differential diagnosis is plantar fasciitis (7). Plantar fasciitis usually presents a pain and symptoms not related to neural compression (7). To avoid a trap, one must keep in mind the cause of tarsal tunnel syndrome is one that compresses, displaces or touches the nerve (7).

Several causes of tarsal tunnel syndrome can be assessed by ultrasound with the patient static, such as

accessory ossicles, synovitis, ganglion cysts, gout, muscular hypertrophy, foreign bodies, and postoperative changes. However, vascular causes, as in the case depicted, require dynamic assessment, and in the case of talar dislocation, there is a need for assessment with the patient in orthostasis. If these evaluations are not carried out, the diagnosis of the cause of tarsal tunnel syndrome will not be made (7).

There is no accurate treatment for tarsal tunnel syndrome caused by a pulsatile tibial artery. Performing conservative treatment helps to establish a good relationship with the patient and allows the surgeon to evaluate the patient for a period to see improvement and observe adherence (9). The objective of conservative treatment is to reduce pain and inflammation and relieve strength, compressive in the tibial nerve (9). The medication often used consists of oral non-steroidal anti-inflammatory drugs (NSAIDs) or analgesic paracetamol in many situations (9). Gabapentin, pregabalin, and tricyclic antidepressants are other oral options for pain relief, and topical medications, including NSAIDs and lidocaine may be helpful (9). Calf muscle strengthening and stretching exercises can aid tissue mobility and nerve mobility/gliding, as demonstrated in one of our cases (9). If conservative measures are not effective, surgical release treatment should be instituted (9). In cases of association with varicosities, the use of compressive socks aids to solve the symptoms, as shown in one of our cases.

Kim et al injected 0.5 mL of 0.5% lidocaine under ultrasound guidance at the site of nerve compression by the tibial artery (2). After the injection, the patient reported immediate resolution of the spontaneous paresthesia (2). However, this effect lasted a few minutes, with a gradual return of the usual symptoms (2). Six months later, she continued to have the same degree of mild paresthesia, without any worsening or improvement (2).

For all etiologies of tarsal tunnel syndrome, conservative treatment (rest, walking boot, shoe wear modifications, physical therapy, ice application, anti-inflammatory medication, strengthen the intrinsic and extrinsic muscles of the foot, anti-neuropathic pain medications, heat, and ultrasound) should be initiated before surgery. Also, weight loss for obese patients. In cases of nerve compression with a space-occupying lesion, surgical decompression in indicated. Timing of surgical intervention is also relevant, as chronic nerve compression leads to axonal loss and intraneural fibrosis, which can be responsible for muscle wasting (10). Endoscopic tarsal tunnel decompression is a safe procedure has a low rate of recurrence or failure despite allowing for near immediate ambulation (11).

CONCLUSION

The reported cases demonstrate two cases of tarsal tunnel syndrome caused by vascular problems, pulsatility and tortuosity of the tibial artery and varicose plantar veins, two commonly misdiagnosed etiologies which needs the attention of the sonographer to diagnose the cause of tarsal tunnel syndrome and offer the adequate treatment.

FUNDING

CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

REFERENCES

1. Nagaoka M, Matsuzaki H. Ultrasonography in tarsal tunnel syndrome. J Ultrasound Med 2005; 24(8): 1035–40.
2. Kim E, Childers MK. Tarsal tunnel syndrome associated with a pulsating artery: effectiveness of high-resolution ultrasound in diagnosing tarsal tunnel syndrome. J Am Podiatr Med Assoc 2010; 100(3): 209–12.
3. Fantino O. Role of ultrasound in posteromedial tarsal tunnel syndrome: 81 cases. J Ultrasound 2014; 17(2): 99–112.
4. Tawfik EA, El Zohiery AK, Abouelela AAK. Proposed sonographic criteria for the diagnosis of idiopathic tarsal tunnel syndrome. Arch Phys Med Rehabil 2016; 97(7): 1093–9.
5. Khodatars D, Gupta A, Welck M, Saifuddin A. An update on imaging of tarsal tunnel syndrome. Skeletal Radiol 2022; 51(11): 2075–95.
6. Samarawickrama D, Therimadasamy AK, Chan YC, Vijayan J, Wilder-Smith EP. Nerve ultrasound in electrophysiologically verified tarsal tunnel syndrome. Muscle Nerve 2016; 53(6): 906–12.
7. de Souza Reis Soares O, Duarte ML, Brasseur JL. Tarsal Tunnel Syndrome: An Ultrasound Pictorial Review. J Ultrasound Med 2021; 41(5): 1247–72.
8. Tajiri T, Kim K, Isu T, Fujihara F, Kitamura T, Takahashi T, Suzuki T, Isobe M, Inoue T. Impact of Dynamic Change of Meandering of Parallel Artery to the Idiopathic Tarsal Tunnel Syndrome. Neurol Med Chir (Tokyo) 2023; 63(4): 165–71.
9. Nelson SC. Tarsal Tunnel Syndrome. Clin Podiatr Med Surg 2021; 38(2): 131–41.
10. Doneddu PE, Coraci D, Loreti C, Piccinini G, Padua L. Tarsal tunnel syndrome: still more opinions than evidence. Status of the art. Neurol Sci 2017; 38(10): 1735–9.
11. Gkotsoulias EN, Simonson DC, Roukis TS. Outcomes and safety of endoscopic tarsal tunnel decompression: a systematic review. Foot Ankle Spec 2014; 7(1): 57–60.