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CASE REPORT

Bridging treatment for antibiotic efficacy in respiratory failure caused by Mycoplasma Pneumoniae infection

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Abstract

Community-acquired pneumonia (CAP) is a common respiratory infectious disease, in 7.5% of cases the responsable pathogen is represented by Mycoplasma Pneumoniae, 4% of these patients require hospitalization in Intensive Care Unit (ICU). We describe two cases of two young male patients with acute respiratory failure caused by Mycoplasma pneumoniae. They were admitted to the ICU with a high risk of requiring intubation, but this was avoided through an individualized treatment. The first case underscores the potential efficacy of high-flow nasal oxygen, supported by esophageal pressure swing (ΔPes) monitoring, evaluating the patient's respiratory effort and titrating the oxygen therapy administered. In the second case, the patient's hypoxemia was treated with high-flow oxygen therapy with inhaled nitric oxide guided by a high shunt fraction. Through the analysis of these two cases, we emphasize the crucial importance of personalized management of hypoxemia in severe instances, as a bridge treatment while waiting for antibiotic therapy to be effective. Additionally, despite the patients not requiring intubation, it is imperative to admit and manage severe cases in ICU. This approach facilitates close monitoring and the potential for therapeutic escalation, ensuring comprehensive care for optimal patient outcomes. Further research is warranted to elucidate the optimal approach to non-invasive respiratory support and prevention of patient self-inflicted lung injury in the early stages of acute hypoxemic respiratory failure. Further researches are needed to assess the efficacy of inhaled nitric oxide in preventing tracheal intubation.

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Introduction

Community-acquired pneumonia (CAP) represents a frequent respiratory infectious disease, with general incidence ranges between 1 and 25 cases per 1000 inhabitants per year. Approximately 40% of patients with CAP require hospitalization, and 5% of these patients require hospitalization in intensive care unit (ICU), due to septic shock or the need for invasive or non-invasive mechanical ventilation [1].

Streptococcus pneumoniae is the most common pathogen (20.0%), followed by *Haemophilus influenzae* (10.8%), *Mycoplasma pneumoniae* (7.5%) and *Chlamydophila pneumoniae* (3.3%); less common are *Moraxella catarrhalis* (2.0%), *Staphylococcus aureus* (1.9%) and Influenza Virus (0.7%) [2]. Mycoplasma pneumoniae infection is more common in children than in adults; in a recent review the proportion of infection between children and adult is 24,5% versus 3,9% [3]. Only 4% of Mycoplasma pneumonia patients need ICU admission for acute respiratory failure.

Mycoplasma pneumonia can progress to acute respiratory distress syndrome (ARDS) and potentially lead to a fatal outcome, particularly when diagnosis and treatment are delayed or respiratory support is inadequate [4]. According to the latest international guidelines for CAP, high-flow nasal oxygen (HFNO) is recommended for patients with acute hypoxemic respiratory failure (AHRF) due to CAP, provided intubation is not immediately required [5]. Evidence indicates that HFNO offers superior oxygenation and reduces respiratory rate compared to standard oxygen therapy. Additionally, a multicenter trial demonstrated that patients with a PaO2/FiO2 ratio ≤ 200 mmHg treated with HFNO had a lower intubation rate compared to those receiving standard oxygen therapy, and even non-invasive ventilation (NIV) via facial mask [6]. However, patient self-inflicted lung injury (P-SILI) may occur when the inspiratory effort in spontaneous breathing is excessive [7]. This effort can be evaluated by measuring the esophageal pressure swing (ΔPes) using a specialized nasogastric tube equipped with an esophageal balloon, with low and high inspiratory efforts defined as ΔPes ≤ 10 cmH2O and >15 cmH2O, respectively [6,8].

Assessing a patient's respiratory effort is crucial to prevent non-invasive treatment failure and subsequent delayed intubation [9-10].

The utilization of inhaled nitric oxide (iNO) has been demonstrated to play a role in enhancing oxygenation in AHRF by improving the ventilation-perfusion mismatch [11]. However, this does not translate into a statistically significant benefit in mortality. This lack of impact on survival may be attributed to the fact that nitric oxide (NO) does not directly influence lung function, reduce lung injury, or resolve the underlying cause of acute respiratory failure, rendering its benefits transient [12]. This topic has attracted considerable attention during the recent COVID-19 pandemic, with evidence suggesting its efficacy as a rescue therapy in moderate-to-severe acute respiratory distress syndrome (ARDS) [13]. Nonetheless, its application as an early intervention in spontaneously breathing patients remains relatively underexplored.

We describe two cases of acute respiratory failure caused by Mycoplasma pneumoniae pneumonia in two young men. They were admitted to the ICU with a high risk of requiring intubation due to hypoxemia, dyspnea, and rapid clinical deterioration [14], but this was avoided through an individualized bridge treatment. Informed consent was obtained from the patients for the use of the data for scientific research purposes.

Clinical case 1

A 20-year-old personal trainer, with a history of hypothyroidism and an allergy to clarithromycin, developed flu-like symptoms following a recent trip to Spain. After a week of persistent high fever, cough, and worsening tachypnea, he presented to the emergency department, where a CT scan revealed bilateral pneumonia with a tree-in-bud pattern. Empirical broad-spectrum antibiotic therapy with Levofloxacin and Ceftriaxone was initiated.

Arterial blood gas analysis (ABG) demonstrated hypoxemic respiratory failure without hypercapnia (PH 7.57 Pa02 44.7 mmhg PC02 25.6 mmhg, Fi02 30%). AHRF did not respond to oxygen therapy with a reservoir mask, with a respiratory rate (RR) of 35-40 breaths per minute.

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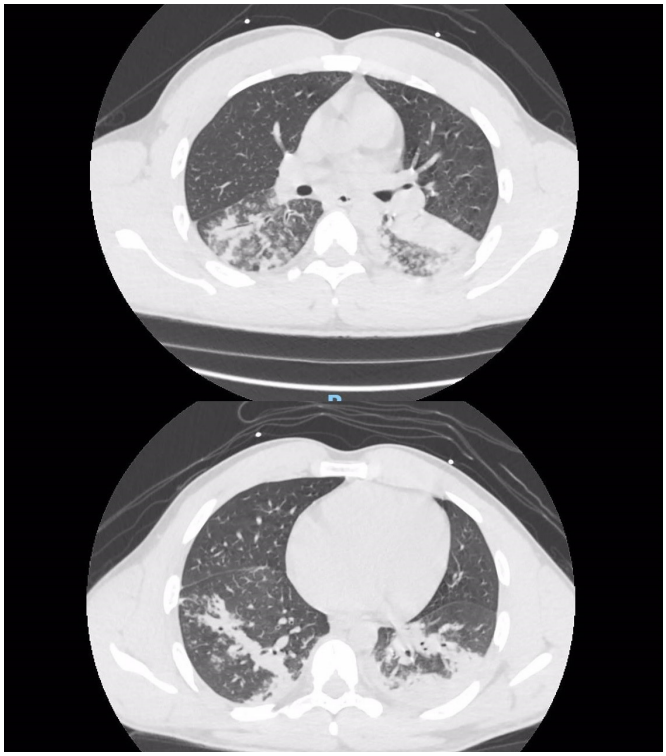
An angio-TC scan was performed, showing a worsening bilateral pneumonia. (**Figure 1**)

FIGURE 1



Subsequently, the patient was admitted to the ICU and HFNO (50l FiO2 50%) was initiated. A nasogastric tube with an esophageal pressure transducer was inserted to measure ΔPes. After the placement of the nasogastric tube, the initial esophageal pressure value was 14; we evaluated all factors that can contribute to an increase in swing, such as agitation, fever, and hypoxia. After initiating mild sedation, managing hyperpyrexia, and increasing the inspiratory fraction of oxygen to 65%, the esophageal pressure rapidly decreased to values between 10 and 12. Over a 12-hour period of HFNO treatment, a reduction in ΔPes from 10-12 to 8 cmH20 was observed. Additionally, arterial blood gas analysis demonstrated progressive improvement in PaO2/FiO2 ratio (P/F) from 147 to 204 mmHg with a reduction in FiO2 to 50%, while maintaining normocapnia. The patient's respiratory discomfort decreased with resolution of fever and tachypnea, and oxygen therapy was transitioned to low-flow nasal cannula. (**Table 1**)

During the ICU stay, a PCR test for Mycoplasma pneumoniae on a nose-throat swab returned positive. Targeted therapy with Levofloxacin was continued, and the patient was transferred to the internal medicine department the following days.

TABLE 1

	Start	30min after mild sedation and treatment of hyperpyrexia	12h Treatment	24h Treatment	30h Treatment
	HFNC 50L/min FiO2 50%	HFNC 50L/min FiO2 65%	HFNC 50L/min FiO2 65%	HFNC 50L/min FiO2 50%	HFNC 50L/min FiO2 50%
TC °C	38	37	37	36	36
pH	7.45	7.44	7.45	7.45	7.45
pCO2	36.9	38.5	37	36	36
P/F	124	147	183	184	204
ΔPes	14	10-12	8	8	8
RR	35		15	14	13

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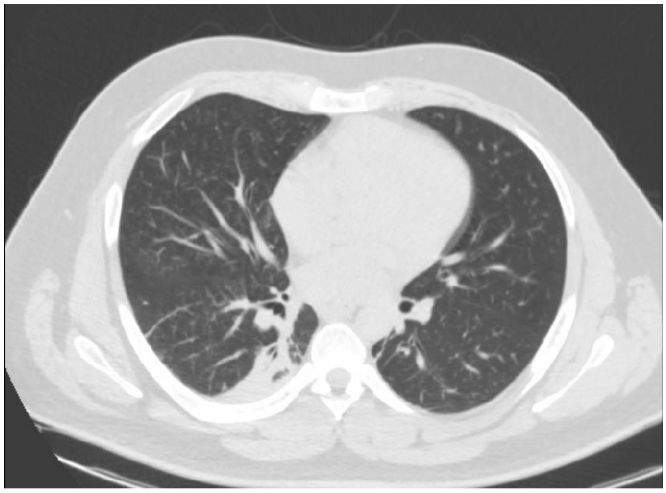
Clinical case 2

A 26-year-old obese man with a history of insulin resistance managed with metformin therapy presented to the emergency department with persistent cough and fever, which worsened despite antibiotic therapy with ceftriaxone. In the previous days, he also experienced an episode of acute urinary retention, necessitating the placement of a urinary catheter. Blood tests revealed neutrophilic leukocytosis with a slight elevation in serum C-reactive protein (CRP) but not procalcitonin (PCT).

A CT scan showed right lobar lung consolidation and a bilateral dorso-basal tree-in-bud pattern. (**Figure 2**) His ABG shows: PH 7.45 Pa02 64.1 mmhg PC02 41 mmHg, with Fi02 60% and RR 30 breaths per minute.

FIGURE 2



Initial attempts at low-flow oxygen administration via Ventimask and then via a mask with a reservoir led to further deterioration with tachypnea and desaturation to SpO2 88%, causing patient exhaustion and necessitating ICU admission.

Broad-spectrum antibiotic treatment with amoxicillin/clavulanate and clarithromycin was initiated.

A subsequent CT scan revealed worsening lung consolidation with a widespread bronchiolitis pattern and areas of air trapping in the superior lobes.

In the ICU, High Flow Nasal Cannula (HFNC) oxygenation was initiated concurrently with nitric oxide administration, starting at 20 ppm, guided by a high shunt fraction (calculated as PaO2/PAO2 < 0.2). iNO therapy had no haemodynamic impact on the patient; assessment of respiratory effort was not available in this patient. Multiplex PCR examination of a nasal swab confirmed Mycoplasma pneumoniae infection on the first day of ICU stay, leading to the discontinuation of penicillin derivatives and continuation of macrolide antibiotic therapy. Despite the severity of his condition, orotracheal intubation was not required during the ICU stay. Following an initial phase of worsening oxygenation and PaO2/FiO2 ratio, the patient exhibited significant clinical improvement, disappearance of subjective dyspnea and normalization of sensorium, stabilization of vital parameters, and a reduction in shunt fraction on the second day. This allowed for the gradual reduction of oxygen support and nitric oxide until their discontinuation. The patient was transferred to a low-intensity care unit on the same day with low-flow oxygen via Ventimask. (**Table 2**)

TABLE 2

	Basal	6h of treatment	12h of treatment	24h of treatment	36h of treatment
	Ventimask FiO2 60%	HFNC 50L/min FiO2 50%	HFNC 40L/min FiO2 40%	HFNC 40L/min FiO2 40%	HFNC 40L/min FiO2 30%
TC °C	36,2	36,3	36,1	36,3	36
pH	7,45	7,47	7.45	7.46	7.4
pCO2	41	36,1	43,6	40,5	45,9
Pa02/PA02	0,17	0,25	0,37	0,27	0,57
P/F	106	161	215	160	302
iNO (ppm)	-	20	10	5	5
RR	30	11	13	24	16

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Discussion

There are no clinical cases in the literature regarding individualized treatments for Mycoplasma pneumoniae infection while awaiting the efficacy of antibiotic therapy; with appropriate respiratory support and anti-mycoplasmal therapy, all patients had a rapid clinical improvement.

This is the first case series that describes two different treatments for two distinct clinical presentations, protecting patients from potential damage due to hypoxemia and non-invasive ventilation.

The first case underscores the potential efficacy of HFNO, supported by ΔPes monitoring, in the management of severe pneumonia complicated by AHRF. The utilization of non-invasive respiratory support in the early management of acute hypoxemic respiratory failure remains a topic of debate. There is evidence suggesting that HFNO may reduce the need for endotracheal intubation, particularly in patients with a PaO2/FiO2 ratio (P/F) ≤ 200 mmHg [5]. Spontaneous breathing may offer multiple benefits in patients with AHFR, including decreased need for sedation, preserved diaphragm activity, improved cardiovascular function, prevents complications associated with endotracheal intubation and invasive mechanical ventilation. However, excessive effort to breathe due to high respiratory drive may lead to P-SILI. High transpulmonary pressure during inspiration and large tidal volumes determine an increase in lung stress and strain [15]. To mitigate this risk, the assessment of inspiratory effort can be performed through measurement of esophageal pressure swing (ΔPes). As the ΔPes values indicated normal to low inspiratory effort, HFNO treatment could be continued leading to an improvement in oxygenation without lung damage and with patient's comfort.

Instead, the second case describe how the use of iNO in spontaneously breathing patients could be a bridge of treatment waiting the response to the antibiotics. While iNO has been extensively evaluated as a rescue therapy in mechanically ventilated patients with ARDS, the effects on patients outcomes in spontaneously breathing patients with AHRF due to causes other than Covid-19 are not well described [16]. INO with its property to improve the ventilation-perfusion mismatch, may serve ad alternative or as a bridge to gain time for lung healing; it also has a potential bronchodilator, anti-inflammatory and potentially direct antimicrobial effect [11].

However, this case highlights its potential early application in acute respiratory failure, potentially averting the need for mechanical ventilation.

Conclusion

Mycoplasma pneumonia is characterized by its atypical clinical and radiological presentation. Through the analysis of these two cases, we emphasize the crucial importance of personalized management of hypoxemia in severe instances, using a continuous monitoring of effort by Pes and the use of a selective vasodilator that may optimize ventilation/perfusion matching increasing oxygenation, while awaiting the effect of antibiotic therapy. Additionally, despite the patients not requiring intubation, it is imperative to admit and manage severe cases in ICU. This approach facilitates close monitoring and the potential for therapeutic escalation, ensuring comprehensive care for optimal patient outcomes. Further research is warranted to elucidate the optimal approach to non-invasive respiratory support and prevention of P-SILI in the early stages of AHRF. Further researches are needed to assess the efficacy of inhaled nitric oxide in preventing tracheal intubation.

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CASE REPORT

A singular use of PEEP during Thermal Ablation of a Lung Lesion Adjacent to the Aorta: A Case Report

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Abstract

Background: Thermal ablation is a minimally invasive procedure commonly performed for treating pulmonary lesions. However, its application near critical structures such as the aorta poses significant challenges, requiring precise anesthetic and procedural management. This report describes the anesthetic and procedural management of a 58-year-old woman with a pulmonary lesion near the aorta, who underwent thermal ablation under one-lung ventilation (OLV).

Methods: The patient, with a prior history of moderately differentiated adenocarcinoma and Takotsubo syndrome, was scheduled for thermal ablation of a 6 mm nodule in the left lower lung lobe. Preoperative evaluation revealed no significant coronary lesions. Under general anesthesia, OLV was established, and the left lung was excluded from ventilation to immobilize the lung. After needle for thermal ablation positioning, the aorta resulted into the thermo ablation area. Critical positive pressure application to the left lung was used to displace the aorta away from the ablation field.

Results: The application of continuous positive airway pressure of 5 cmH_2O was applied to the non-ventilated left lung resulted in an 8.19 mm displacement of the aorta, enabling safe thermal ablation without damaging critical structures. Intraoperatively, the patient remained stable, and postoperatively, she was discharged uneventfully after 3 days.

Conclusions: This case highlights the importance of multidisciplinary collaboration and tailored anesthetic management in high-risk procedures involving pulmonary lesions near critical vascular structures. OLV with selective intubation, combined with careful positive pressure application, played a crucial role in ensuring procedural safety.

Keywords: non-operating room anesthesia, mono pulmonary ventilation, PEEP, thermal ablation.

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Introduction

Thermal ablation is a widely used, minimally invasive treatment for small pulmonary lesions, particularly in cases where due to the patients' severe medical comorbidities, surgery is frequently a high-risk procedure. It offers a less invasive alternative to surgical resection, with reduced recovery time and lower morbidity. However, the particular characteristics of the tissue determine the extent of ablation that can be accomplished. In such cases, continuous blood and airflow next to the target in the lung parenchyma is the most crucial component to take into account, especially when the lesion is located near critical structures, such as the aorta or other major vessels [1,2]. Ensuring patient safety while maintaining procedural efficacy requires meticulous perioperative optimisation, planning and innovative anesthetic strategies which may increase the likelihood of a desirable outcome for the patient [3].

This case report presents the anesthetic management of a 58-year-old female patient undergoing thermal ablation of a pulmonary lesion situated in close proximity to the aorta. The complexity of the procedure was further compounded by the risk of vascular injury due to the lesion's location, necessitating the displacement of the aorta from the ablation field. This was achieved through an innovative application of positive pressure to the non-ventilated lung, which played a critical role in ensuring the safety and success of the ablation.

Case Presentation

A 58-year-old woman, with a 30-year history of smoking and a family history of hepatic neoplasia, presented to the emergency department in September 2023. She reported foul-smelling vaginal discharge, resembling fecaloid material. A gynecological examination revealed an irregular mass on the posterior vaginal wall, approximately 2 cm in diameter. A biopsy performed during colonoscopy confirmed moderately differentiated ulcerated adenocarcinoma. Surgery and radiotherapy were ruled out as first-line therapeutic options. During the first cycle of chemyotherapy, she developed angina, caused by Tako-Tsubo syndrome. During follow-up hospitalization, a contrast-enhanced CT scan identified a new solid nodule, 6 mm in size, in the apical segment of the left lower lobe of the lung. A PET scan confirmed the lesion's malignancy. Following multidisciplinary discussions, thermal ablation was proposed as a feasible treatment, provided the anesthetic evaluation supported the procedure. Due to the proximity of the lesion to the aorta, general anesthesia with one-lung ventilation (OLV) was determined to be the safest approach. Selective left-sided orotracheal intubation was planned to enable exclusion of the left lung from ventilation, thus providing optimal surgical conditions for thermal ablation near the aorta. The patient was prepared for the procedure with continuous monitoring, including non-invasive blood pressure measurements at five-minute intervals, pulse oximetry, continuous ECG, end-tidal CO_2, and bispectral index (BIS) monitoring to assess anesthetic depth. General anesthesia was induced in the post-anesthesia care unit (PACU) with propofol target-controlled infusion (TCI- Schnider effect-site) and remifentanil (Minto model effect-side). Muscle relaxation was achieved rocuronium. Once the patient reached a BIS value of 50, a size 37 double-lumen endotracheal tube was inserted using a GlideScope® video laryngoscope, with placement confirmed via fibroscopy.

The patient was transported from the PACU to the radiology suite, where the thermal ablation would be performed under CT guidance. She was positioned on her right side. Prior to commencing the thermal ablation, the anesthesiologist excluded the left lung from ventilation. Imaging revealed that the lesion, situated in the apical segment of the left lower lobe, was dangerously close to the aorta (**Figure 1**) This proximity posed a significant risk for potential damage to the aorta during ablation. To mitigate this risk, continuous positive airway pressure (CPAP) of 5 cmH_2O was applied to the non-ventilated left lung, causing mild lung expansion and displacing the aorta away from the ablation field by 8.19 mm (**Figure 2**). This displacement more than doubled the safety margin between the aorta and the targeted lesion, significantly reducing the risk of vascular injury.

The radiology team successfully performed the thermal ablation without further complications. The positive pressure applied to the non-ventilated lung proved essential for creating the necessary space between the aorta and the ablation site, ensuring the procedure's safety.

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At the end of the procedure, the tube was removed and the patient monitored in the PACU for two hours before being discharged to the ward. She exhibited stable vital signs and no adverse events. A chest X-ray showed good expansion and ventilation in both lungs, with no evidence of pleural effusion.

FIGURE 1 - CT scan image before applying positive pressure to the non-ventilated left lung.

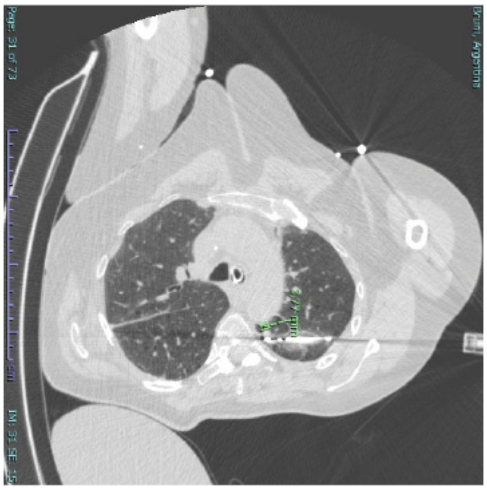
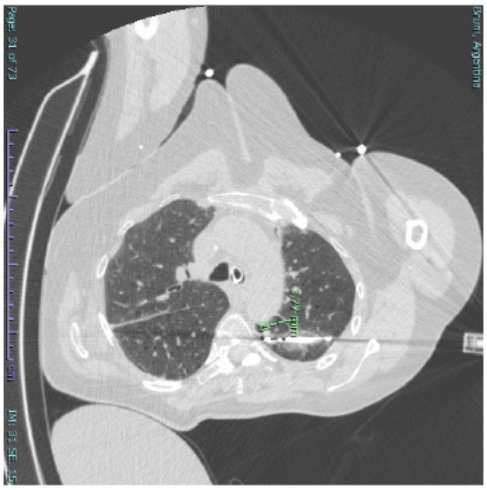


FIGURE 2 - CT scan image after applying positive pressure to the non-ventilated left lung.



Discussion

Image-guided thermal ablation is a reliable and safe technique for managing lung metastases from colorectal cancer. With careful patient selection, this approach can extend survival and reduce the need for chemotherapy. Emerging in the early 2000s, percutaneous thermal ablation offers a minimally invasive alternative to surgery for patients who are either ineligible for surgical intervention or seeking to preserve their quality of life [4]. Numerous studies have demonstrated improved overall survival and progression-free survival following local ablative therapy for carefully selected pulmonary metastases, compared to optimal medical therapy [5].

Thermal ablation of pulmonary lesions located near vital structures, such as the aorta, presents substantial challenges. Effective anesthetic management must ensure both optimal procedural conditions and the utmost patient safety, particularly when the proximity of critical vascular structures increases the risk of inadvertent injury. In this case, the ablation of a lesion located close to the aorta required a highly innovative and flexible approach to maintain procedural safety while achieving complete lesion removal.

The use of one-lung ventilation (OLV), with selective intubation, is a well-established technique in thoracic surgery to isolate a lung for surgical intervention. However, its use in a radiological setting, outside of the traditional operating room, highlights the adaptability and necessity of tailored anesthetic approaches in complex, minimally invasive procedures. The anesthetic strategy employed in this case was particularly innovative due to the critical role of continuous positive airway pressure (CPAP) applied to the non-ventilated lung. This intervention was pivotal in providing a safe margin for the ablation.

The application of CPAP to the non-ventilated left lung was essential not just for procedural facilitation, but for enhancing patient safety. By applying a controlled positive pressure of 5 cmH_2O, the anesthetic team successfully expanded the lung slightly, which resulted in a significant displacement of the aorta from the lesion. This maneuver increased the distance between the aorta and the targeted lesion by 8.19 mm, more than doubling the initial safety margin. Such a displacement was critical in minimizing the risk of thermal damage to the aorta during the ablation process. The use of CPAP and PEEP is also effective in treating hypoxia and atelectasis resulting from one-lung ventilation and they play a crucial role in a protective lung ventilation strategy to mitigate mechanical stress and prevent acute lung injury. CPAP and PEEP are becoming increasingly important when faced with patients who have reduced respiratory reserve and

greater comorbidity, requiring more comprehensive clinical management and additional interventions to prevent perioperative complications [6].

This approach underscores the importance of real-time adaptability in anesthetic management, especially in high-risk cases where the proximity of critical structures makes conventional approaches insufficient. By using CPAP on the excluded lung, the anesthesia team not only facilitated the procedure but also actively altered the anatomical landscape, creating a safer environment for the radiologist to perform the ablation. Without this innovative approach, the risk of inadvertent injury to the aorta would have been significantly higher, potentially leading to catastrophic complications such as vascular rupture or uncontrolled bleeding.

Moreover, the successful use of CPAP in this case provides a valuable precedent for similar high-risk procedures. While OLV is typically employed to prevent lung movement and protect structures, the deliberate and controlled re-expansion of the excluded lung in this case was an essential modification. This intervention appeared to facilitate the careful manipulation of the lesion's relationship to critical vascular structures, potentially making the procedure feasible in a situation that might have otherwise been considered too risky. In this particular case, the application of CPAP to the non-ventilated lung not only displaced the aorta but also provided a stable anatomical shift, enabling the radiology team to proceed with the ablation.

The decision to apply CPAP illustrates a fundamental principle in anesthetic management: maintaining flexibility and control over patient physiology to meet the demands of complex procedures. The collaboration between the anesthesiology and radiology teams was paramount in this case, as the anesthetic strategy directly influenced the procedural success. The real-time adjustments made by the anesthesia team, specifically the use of CPAP to manipulate the proximity of the lesion to the aorta, were integral to ensuring both the safety and efficacy of the thermal ablation. Additionally, this case highlights the broader implications of anesthetic management in non-operating room anesthesia (NORA) settings. NORA procedures have grown significantly over the years, along with the increasing complexity and severity of cases. Administering anesthesia in these often unfamiliar environments carries inherent risks, and complications are not uncommon. Providing anesthesia outside of traditional operating rooms presents unique challenges. However, thorough planning, close communication with the procedural team, the development of clear protocols and support pathways, combined with strong interdisciplinary teamwork, can help ensure safe, efficient, and cost-effective care in the NORA setting [7,8].

The use of CPAP in this case represents a novel application of a conventional technique, demonstrating how NORA settings require a versatile, patient-centered approach to anesthesia.

Conclusion

In conclusion, the application of CPAP to the non-ventilated lung appears to have contributed to making this high-risk procedure more manageable. This case underscores the importance of precise and adaptable anesthetic management in complex procedures involving pulmonary lesions near major vascular structures. By applying positive pressure to the excluded lung, the anesthesia team helped create conditions for the radiology team to perform thermal ablation without compromising the integrity of the aorta. This case emphasizes the value of multidisciplinary collaboration, innovative thinking, and the critical role of anesthetic techniques in high-risk, minimally invasive procedures. While the outcome was successful, further evidence is needed to confirm the broader applicability of this approach.

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ORIGINAL ARTICLE AND META-ANALYSIS

The "Vascular Donut Sign": when a thrombus envelops the fibrin sheath

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Abstract

Catheter-related thrombosis is a common condition associated with various complications. In many cases, what appears to be catheter-related thrombosis is actually a fibrin sheath. Ultrasound examination serves as an effective diagnostic tool, particularly when a specific and intriguing ultrasound marker can aid in differentiation. Here, we present a clinical case that highlights this ultrasound marker, known as the "Vascular Donut Sign".

Keywords: Catheter-related thrombosis, ultrasound examination, fibrin sheath, "Vascular Donut Sign"

Introduction

Central venous catheters (CVCs) are essential devices in the management of critically ill patients in the intensive care unit (ICU). The most common catheter-related complications include mechanical, septic, and thrombotic events. Thrombotic complications, among the most feared, may lead to pulmonary embolism, upper sagittal sinus thrombosis, intracranial hypertension, edema, septic embolism, chylothorax, and superior vena cava syndrome [1]. The risk of thrombosis associated with internal jugular vein (IJV) catheters is four times higher than that of subclavian vein catheters. Approximately 66% of patients with IJV catheters exhibit evidence of thrombus formation on ultrasound or autopsy [2]. Thrombi can develop along the entire length of the IJV, from the puncture site to the subclavian vein [3]. Ultrasonography (US), particularly with color Doppler, is a non-invasive and readily available tool capable of detecting intraluminal thrombi at early

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stages. Additionally, US can help distinguish between true thrombi and fibrin sheaths, although both may coexist. Does ultrasound imaging enable precise diagnosis in such scenarios? We present a clinical case featuring a distinctive ultrasound marker, termed the "Vascular Donut Sign," resulting from unilateral IJV thrombosis with a fibrin sheath.

Clinical Case

A 72-year-old patient with a history of arterial hypertension, type II diabetes mellitus (on oral hypoglycemic therapy with suboptimal glycemic control), and peripheral vasculopathy (with previous right thigh amputation) was admitted to the ICU for suspected metformin intoxication and sepsis. During hospitalization, the patient was diagnosed with a right colonic tumor abscess, which subsequently led to septic shock.

Upon ICU admission, an arterial catheter was placed in the left radial artery, and a CVC was inserted into the right IJV under ultrasound guidance (due to inadequate axillary vein diameter). The clinical pretest probability of deep vein thrombosis, assessed using the Wells score (>2), indicated a high risk of thrombosis [4]. Compression ultrasound (CUS) of the jugular, subclavian, and bilateral axillary veins showed complete venous wall collapse without endoluminal material. Bilateral femoral CUS revealed hyperechoic endoluminal material with partial coaptation in the right femoral vein.

The patient's sepsis, caused by an extended-spectrum beta-lactamase (ESBL)-producing strain of Escherichia coli, was treated with initially empirical and subsequently with targeted antibiotic therapy. Severe sepsis-related thrombocytopenia prompted the initiation of reduced-dose prophylactic anticoagulant therapy (enoxaparin 4000 IU/day subcutaneously).

The onset of anuria and electrolyte imbalances due to severe renal failure necessitated continuous veno-venous hemodiafiltration (CVVHDF). A GamCath Dual-lumen© hemodialysis catheter was then placed in the left femoral vein. Ultrasound evaluation (using the RAFEVA and RACEVA protocols) was performed with a linear probe (5.3–10 MHz) in B-mode, optimizing image depth and attenuation [5,6,7]. The evaluation criteria included vein caliber, depth, collapsibility during respiration, proximity to critical structures, and feasibility of emergency site access for catheter management.

Seven days after placement of the dialysis catheter in the left femoral vein, a malfunction of the catheter occurred, necessitating its removal. Therefore, re-potting of the catheter was necessary because the patient still required dialysis treatment. US examination revealed partial thrombosis of the right femoral vein. A CVC had already been inserted into the right jugular vein, while both axillary veins were unobstructed but measured <6 mm in diameter [7,8]. Consequently, the right IJV CVC was replaced with a hemodialysis catheter, and a new CVC was inserted into the left subclavian vein.

Forty-eight hours after catheter placement, ultrasound revealed a unique image - a hyperechoic circular structure with an anechoic center, resembling a concentric "donut" (**Figure 1-2**). This structure extended from the venipuncture site to the ipsilateral innominate vein, with a clear subclavian entry. A centrally inserted central catheter (CICC) was placed in the left subclavian vein, and a dialysis catheter was inserted into the right jugular vein. Based on the hypothesis of a thrombus overlying a fibrin sheath, calcium heparin therapy (10,000 IU/day) was initiated, considering the patient's eGFR <10 mL/min.

The neoformation was monitored by ultrasound at 3, 7, 10, and 14 days and it resolved completely by day 31 (**Figure 3**).

FIGURE 1 - Round fibrin sheat of pericatheter in the internal jugular vein

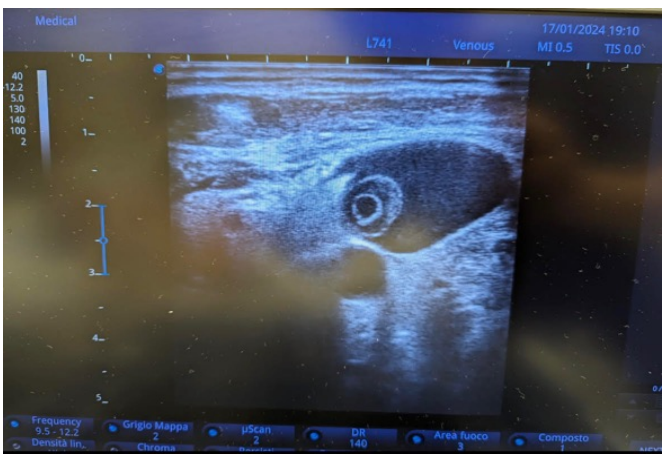

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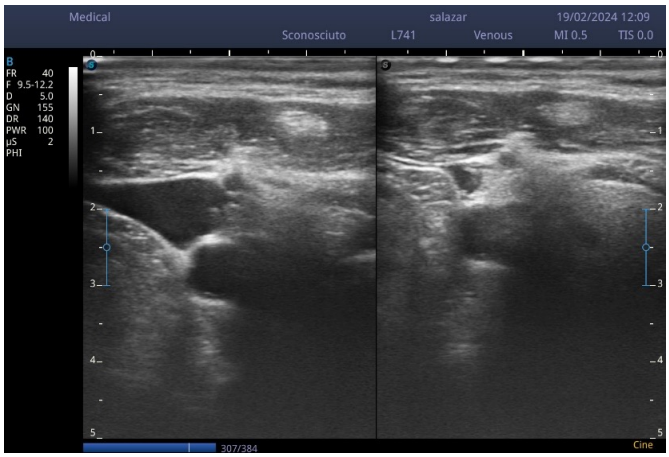
FIGURE 2 - Round fibrin sheat of pericatheter as "Donut's Sign"

FIGURE 3 - Resolution of fibrin sheat in thirty-three-first day



Discussion

This patient exhibited multiple pro-thrombotic risk factors, including septic shock, malignancy, prolonged bed rest, diabetes, vasculopathy, arterial hypertension, and a Wells score >2. CVC placement was performed in accordance with recommendations for preventing catheter-related thrombosis [7].

Thrombosis, once diagnosed, necessitates treatment, with CVC removal guided by clinical circumstances and ultrasound findings. Differentiating a fibrin sheath from a thrombus is crucial for clinical and ultrasound-based decision-making. Catheter-related thrombosis is defined as a mural thrombus encircling the catheter intraluminally, causing partial or total occlusion with or without symptoms. Common symptoms include inflammation and vascular obstruction (e.g., edema, pain). However, as in this case, symptoms may be absent or undetectable.

Catheter-related thrombosis can result in catheter dysfunction, manifesting as aspiration and infusion failure. Thrombus formation is triggered by venous wall damage from catheter insertion or mechanical/chemical trauma, initiating the pro-thrombotic imbalance described by Virchow [9]. Thrombi typically adhere to the vein wall and may partially envelop the catheter. On ultrasound, thrombi appear as rounded, hypoechoic, and compressible structures that can partially or completely occupy the venous lumen [10].

A fibrin sheath, in contrast, forms around the catheter as a foreign-body reaction initiating fibrinogenesis. This sheath consists of fibrinogen, albumin, erythrocytes, fibroblasts, collagen, and smooth muscle cells. Formation begins within 24 hours from catheter insertion [11]. While fibrin sheaths are generally asymptomatic, they may lead to catheter malfunction by creating a one-way valve at the catheter tip, obstructing aspiration while allowing infusion [12]. Ultrasound imaging shows the fibrin sheath as a hyperechoic ring in cross-sectional view or a tubular structure in longitudinal view. Distinguishing a fibrin sheath from thrombus requires correlating clinical findings, ultrasound features, and the time since catheter insertion (24-72 hours for fibrin sheaths vs. ~6 days for thrombi) [12].

The "Vascular Donut Sign" described in this case - a concentric, hypoechoic image with a hyperechoic periphery - represents the coexistence of a fibrin sheath and pericatheter thrombus. Vessel compressibility further aids differentiation, with thrombi becoming increasingly non-compressible over time [13]. Doppler examination of the IJV - including spectral analysis - is crucial for assessing vessel patency and detecting intravascular thrombi. Reduced or absent flow suggests thrombus formation. Comparative evaluation with contralateral veins enhances diagnostic accuracy.

In this case, the absence of IJV thrombotic symptoms or CICC malfunction underscores the importance of routine ultrasound monitoring in high-risk patients.

Conclusion

The "Vascular Donut Sign" observed in this patient reflects the coexistence of a fibrin sheath and pericatheter thrombosis. This pathognomonic ultrasound marker highlights the importance of distinguishing these entities for accurate diagnosis and management (**Figure 3**).

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ORIGINAL ARTICLE AND META-ANALYSIS

Time for a Closer Look at Cardiac Arrest Ventilation

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Background

Out of Hospital cardiac arrest (OHCA) is the sudden cessation of circulation, OHCA has an incidence of about 1 in 1000 inhabitants.[1] OHCA is a primary health problem around the globe.[1] The current overall survival rate is approximately 10%[1]; and depends upon various critical factors, including the location of the incident, the proximity to a first responder, the availability of defibrillation for shockable rhythms, and the quality of bystander cardiopulmonary resuscitation (CPR) [1,2].

Guidelines concur with the practice of maintaining a ventilation rate of 10 breaths per minute following the insertion of a tracheal tube (TT) or a supraglottic airway (SGA) in adult patients [3].

Excessive ventilation during CPR, especially when minute ventilation surpasses 30 liters per minute, significantly reduces patient survival rate [4,5]. In animal experiments with varying ventilation rates (12, 20, and 30 breaths per minute), higher ventilation rates were associated with increased intratracheal pressures, decreased coronary perfusion pressures, and lower survival rates [4,5]. During CPR, lung hyperinflation can mimic cardiac tamponade, impeding circulation [6] and induce hypocapnia, triggering vasoconstriction in brain arteries and diminishing cerebral blood flow, potentially jeopardizing long-term neurological outcomes [7]. EMS clinicians should take measures to prevent hyperventilation during out-of-hospital cardiac arrest (OHCA) resuscitation [8].

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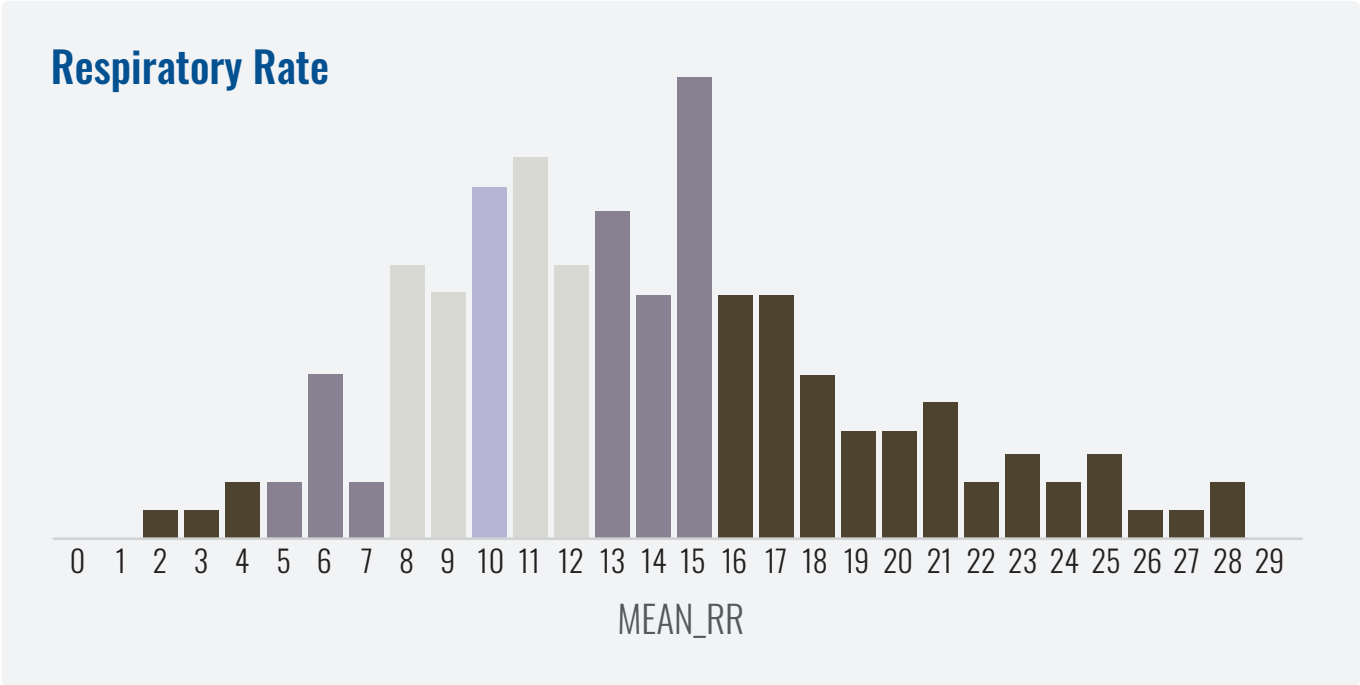
Implementation of study and results

We conducted a retrospective observational study. An analysis was performed in all retraining courses carried out by the SIMED (Italian Society of Medicine and scientific Divulgation) training center in the year 2023, for all subjects who had conducted an American Heart Association (AHA)-certified Basic Life Support and Defibrillation (BLSD) course for healthcare professionals in the period 2021-2022. BLSD course provides training by simulation with manikins. All course participants consented to the study. A dummy capable of recording the respiratory rate (RR) was used. An analysis was conducted on the RR of ventilation performed by healthcare professionals in the first scenario of the course.

We analyzed 159 nurses. Of these, 89 (55.9%) were female, with an average age of 26 years (SD: 2.1). The Respiratory mean Rate record by manikins was 14 (SD: 5.3).

The Interquartile Range was 6.6 and the range was 2-28. The respiratory rate distribution is present in the figure.

FIGURE - Histogram depicting the distribution of respiratory rates during assisted ventilation.



All participants passed the retraining course, with a theory test score of 24.2/25 and SD: 2.2.

According to the guidelines, we divided the trainee performances into slightly out of range (those that provided i.e., 8-9-11-12 ventilation per minute) 42/159 participants (26.4% of the sample) and completely out of range (those that provided less than 8 or more than 12 ventilations) 105/159 participants (66% of the sample). Participants that performed excellently with 10 ventilations per minute (as recommended by the guidelines) were 12/159 participants (7.5% of the sample).

Discussion

This study shows that during a retraining course carried out to certified operators within two years of the first training course, differences with the guidelines can be recorded. This element is very significant and should be investigated further, as the students showed a large level of satisfaction [9] after the courses and demonstrated a greater ability to handle emergencies [2], but not all students showed the same level of performance after two years.

Data indicate a mean respiratory rate of 14 breaths

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per minute during resuscitation efforts underscores a critical issue: the apparent lack of adherence to established guidelines. In the context of cardiac arrest the first aid is essential [10], and an appropriate cardiopulmonary resuscitation is fundamental for the patients outcome [2,10], where optimizing patient outcomes is paramount, the failure to respect recommended ventilation rates is concerning. This departure from the guideline of 10 breaths per minute raises questions about the consistency and quality of care provided during high-stress resuscitation scenarios. Hyperventilation, associated with higher respiratory rates, can compromise coronary perfusion pressure, and hinder the chances of achieving the return of spontaneous circulation (ROSC). The deviation from guidelines is not an isolated incident and other authors have previously reported similar deviations.[6] These findings suggest a broader systemic issue within the field of resuscitation medicine. The recurrent failure to adhere to recommended ventilation rates during CPR underscores the need for a comprehensive review of resuscitation practices and a concerted effort to address these deviations to improve patient outcomes. Consistency in guideline adherence is crucial to ensuring that patients receive the highest quality of care during critical moments of cardiac arrest management.

The analysis of maintenance times for practical skills is a relevant topic for training. In fact, defining the duration of the certification should always be defined and updated together with the guidelines, in fact over the years the training methods are modified and therefore the learning methods could also be different and the memory times of the student guidelines.

Strengths and weaknesses

The research has some noteworthy aspects. Notably, the instructors who conducted both the training and retraining courses were the same individuals, and the training sessions were held at the same center. The retention rate was automatically recorded, and the sample of participants involved in the research was notably relevant.

However, despite these strengths, certain limitations existed. Primarily, it was a single-center study, potentially introducing population selection bias. It's plausible that individuals opting for retraining might either be less prepared, those who have most significantly lapsed in their skill retention or those more interested in the topic. Finally, our investigation delved into a critical aspect of resuscitation one that might inadvertently take a backseat for instructors. Training predominantly emphasizes cardiopulmonary resuscitation over ventilation, despite the latter's significance.

Conclusion

The study underscores a concerning trend: nurses trained in Basic Life Support and Defibrillation (BLSD) may experience a decline in the practical manual skills acquired during their initial training upon retraining. This emphasizes the need for potential revisions not only in updating BLSD guidelines but also in reconsidering certification duration. Additionally, there should be a heightened emphasis placed on ventilation during training courses, recognizing its pivotal role in effective resuscitation efforts.

Acknowledgments

All the research has been conducted adhering to the recommendations contained in the Declaration of Helsinki and it complies with the International Guiding Principles that regulates research activities. All the authors have no Conflict of Interest to declare.

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LETTER TO EDITOR AND EXPERT COMMENTARY

Basic Life Support and Defibrillation course in the Medical School: What is the best year of course to train the students?

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Authors' contributions:
GS conceived and designed the study; MDA collected and analyzed the data; GG and LG, GR and NF interpreted the results of the experiments; LG prepared figures; MDA and GS drafted the first versionof the manuscript. All authors edited and revised the manuscript.All authors have read and agreed to the published version of the manuscript.

Ethics and Informed Consent Statement:
the study was approved by SIMED research board and consensus and information and consent to the processing of personal data was delivered to the participants.

Conflicts of interest:
Professor Giuseppe Ristango is a member of the ERC, Giuseppe Stirparo and Luca Gambolò are ACLS and BLSD instructor

Abstract

BLSD (Basic Life Support and Defibrillation) training is essential to improve the chances of survival in cardiac arrest situations. However, in Italy, BLSD training in medical school is not standardized, and only some universities offer it. A study at the University of Parma surveyed sixth-year medical students' BLSD experience and self-perceived readiness for emergency intervention. Results showed that those who completed BLSD training felt more autonomous and confident in handling cardiac arrest, particularly those who had witnessed such an event. Findings suggest introducing BLSD training early in medical curricula, with additional training before graduation to enhance professional competence in emergency response.

Keywords: Resuscitation, BLSD, Medical Students

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Introduction

Basic life support and defibrillation (BLSD) training is crucial in increasing the likelihood of return to spontaneous circulation (ROSC) of cardiac arrest (CA) patients.[1-4] In this regard, training of next-generation physicians remains a highly relevant but still debated issue, especially when deciding the best year for medical students to take the BLSD course. In fact, not all Italian universities have implemented formal BLSD training as part of the

student curriculum, while no Italian national rules have been established for simulation training.[4,5] For this reason, BLSD training experiences during medical school currently remain only local initiatives in some individual universities.

What would be the most correct year during the Medical School for BLSD training?

In the project developed by a group of university professors, medical education experts, and the SIMED's Scientific Board, the SIMED NewDoc course [6] was defined. The course defines the practical skills of "Newly Licensed Physicians" (NLPs) physicians within 12 months of licensure. The sixth year of medical school appeared the best time to introduce BLSD training. In fact, it is the time when the student is close to graduation and the start of work as a full-fledged physician, but unfortunately demonstrates little autonomy in the management of emergencies, such as cardiac arrest.[7-8] We conducted a single-centre cross-sectional study to understand the opinion and experience of medical students at the University of Parma regarding the above issue. A questionnaire was distributed on a voluntary basis to all sixth-year medical students. Participants were informed of the research and the aim of the questionnaire and gave their consent. The questionnaire included 8 questions related to theoretical knowledge (in accordance with ERC 2021 guidelines) [9] and 3 questions related to previous experience of cardiac arrest (**Figure 1A**).

TABLE 1 - Regression model on self-evaluated autonomy

Variabile	Stima	SE	Z	OR	p value
Sex	-1.653	0.571	-2.893	0.19	0.004
Age	0.047	0.125	0.380	1.05	0.704
Good theoretical knowledge	0.377	0.617	0.612	1.46	0.540
Have you ever witnessed a cardiac arrest?	1.399	0.628	2.229	4.05	0.026
Have you attended a BLSD course?	2.038	0.589	3.460	7.68	<0.001

Results

Ninety-nine students were enrolled, accounting for 43% of all sixth-year students. Fifty-four percent were female and the average age was 25.7+/-2.1 years. Regarding theoretical knowledge, the average score on the questions was 5.8+/-1.4. Sixty-three percent of the students answered at least 6 questions correctly, thus demontrating sufficient theoretical knowledge of the topic. With regard to the three questions on previous experience, 34% of the students had already attended a BLSD course of at least 8 hours; however, only 33% of them felt prepared to intervene in the event of cardiac arrest and 23% had already witnessed a cardiac arrest. Perceived autonomy in managing a cardiac arrest was higher in students who had taken a BLSD course (OR: 8.8, 95% CI 3.4-23.0; p<0.001), and in those who had witnessed a cardiac arrest (OR: 4.6, 95% CI 1.7-12.3; p=0.003). Importantly, of the 23 subjects who had witnessed a cardiac arrest, only 13 (56%) had completed a BLSD course. In order to understand the variables that most influence the perceived autonomy of NLPs, a logistic regression was performed on the variables analysed in the questionnaire. The logistic regression model presented in Fig.1B predicted about 31% of the items influencing the students' perceived

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autonomy in coping with cardiac arrest (model fit measures: Deviance 88.8, AIC 100.8, R2 0.31).

Discussion and conclusion

Having attended a BLSD course increased perceived autonomy even more than having witnessed a cardiac arrest. Gender seemed to influence perceived autonomy, with males showing greater confidence. However, theoretical knowledge had no impact on perceived autonomy. As for age, the range was too narrow to have an impact. Therefore, correct knowledge, from a theoretical standpoint, in the absence of the development of practical skills, does not enable the student to be ready to intervene in the real-world scenario and students appeared to be aware of this phenomenon. Furthermore, those who have conducted a BLSD course generally also have more theoretical knowledge, and thus there may be a collinearity with those who have developed a BLSD course.

This article presents some limitations, including the lack of information regarding the student's school of specialisation, if any, or where he or she is doing his or her thesis internship. In addition, it is possible that those who decided to do the course had a greater propensity for emergency courses. Finally, it would be interesting to compare the result with students at other universities where the course is provided.

This result could be relevant to medical training, since, according to traditional curricula, the most relevant part of the training includes only ward-based internship, in which the student observes daily clinical activity. Whereas, according to this preliminary survey, BLSD training with also simulation could have a greater impact on professional self-autonomy. Interestingly, about a quarter of final-year medical students may have already witnessed a cardiac arrest. Therefore, it would be relevant to discuss whether the BLSD training should be included during the early years of the medical students' curriculum, since they may encounter a cardiac arrest during their ward-based internships or in daily lives. Therefore, in our opinion, it will be optimal to implement undergraduate BLSD training projects at the entrance of medical school with a refresher during the final year.

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SUPPLEMENTARY 1 QUESTIONARY

Gender:
Age:

1 - Indicate the incidence of cardiac arrest in Italy
- 2/1000
- 1/1000
- 5/1000
- 1/10000
- 2/10000

2 - Indicate the main cause of cardiac arrest in Italy
- Ischemic heart disease
- Genetic alterations
- Cardiac hypertrophy
- Major trauma
- Intoxication

3 - Indicate the frequency of chest compressions
- 75-95 Compressions/min
- 120-140 Compressions/min
- 100-120 Compressions/min
- 85-105 Compressions/min
- 105-125 Compressions/min

4 - Indicate the compression-to-ventilation ratio for a patient in cardiac arrest
- 30/5
- 15/2
- 30/1
- 15/1
- 30/2

5 - In the absence of personal protective equipment for mouth-to-mouth resuscitation
- Mouth-to-mouth resuscitation can be omitted
- Mouth-to-mouth resuscitation is always mandatory
- The frequency of breaths compared to compressions is reduced
- A handkerchief or a piece of cloth like a shirt sleeve must be used
- The jaw must be subluxated

6 - How deep should chest compressions be?
- At least 5 cm
- More than 4 cm
- Less than 5 cm
- At least 6 cm
- More than 3 cm

7 - To perform ventilations on an adult subject
- The head must be hyperextended
- The head must be moderately extended
- The head should not be extended
- The head should not be extended to prevent cervical fractures
- The jaw must be subluxated

8 - When should the AED be used?
- As soon as possible
- After 2 minutes
- After two compression cycles
- After 10 minutes
- After 1 cycle of compressions

9 - Have you completed a practical BLSD course of at least 8 hours? Yes - No

10 - Have you ever witnessed a cardiac arrest? Yes - No

11 - Do you feel ready to intervene in front of a patient who goes into cardiac arrest? Yes - No

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EDITORIAL

The advisory board for the implementation of the chain of survival: a leap into the future of lay resuscitation in Italy

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The poor outcomes currently observed in out-of-hospital cardiac arrest (OHCA) are likely attributable to delays in the initiation of cardiopulmonary resuscitation (CPR), ineffective and low-quality chest compressions, and limited or delayed access to defibrillation.[2-3] The Italian Agency for Healthcare Quality (AGENAS) has established an 8-minute call-to-intervention time in urban areas and 20 minutes in rural areas. While the Italian Emergency Medical Services (EMS) generally meets these targets, in the context of cardiac arrest and its associated anoxic cascade,[4-6] resuscitation efforts initiated solely by EMS often occur too late. Consequently, early intervention by laypersons is crucial for improving survival outcomes.

The concept of the *Chain of Survival*, first introduced in 1968, underscores the interdependency of time-critical interventions in cardiac arrest. Adopted by the European Resuscitation Council in 2005, it has since been refined to highlight the relative importance of each link in successful resuscitation efforts.[7] Despite efforts to emphasize the first three links - recognition, calling for help, and early CPR and defibrillation - Italy's rates of lay rescuer-performed CPR and defibrillation remain alarmingly low at 32% and 3.2%, respectively, compared to the European averages of 56.7% and 28%.[1,8,9]

To address these disparities and promote a culture of resuscitation among laypersons, the Italian Resuscitation Council (IRC) launched the *Advisory Board for the Chain of Survival* in December 2023. This advisory board comprises nine members, including healthcare professionals experienced in public CPR education and lay rescuers actively engaged in cardiac arrest awareness initiatives.

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The board's first meeting with the IRC steering committee occurred in January 2024, focusing on prioritizing the implementation of the Chain of Survival across four key settings: schools, sports, workplaces, and institutional advocacy. Among these, school-based education was identified as the top priority.

The following key objectives were outlined **(Figure 1)**:

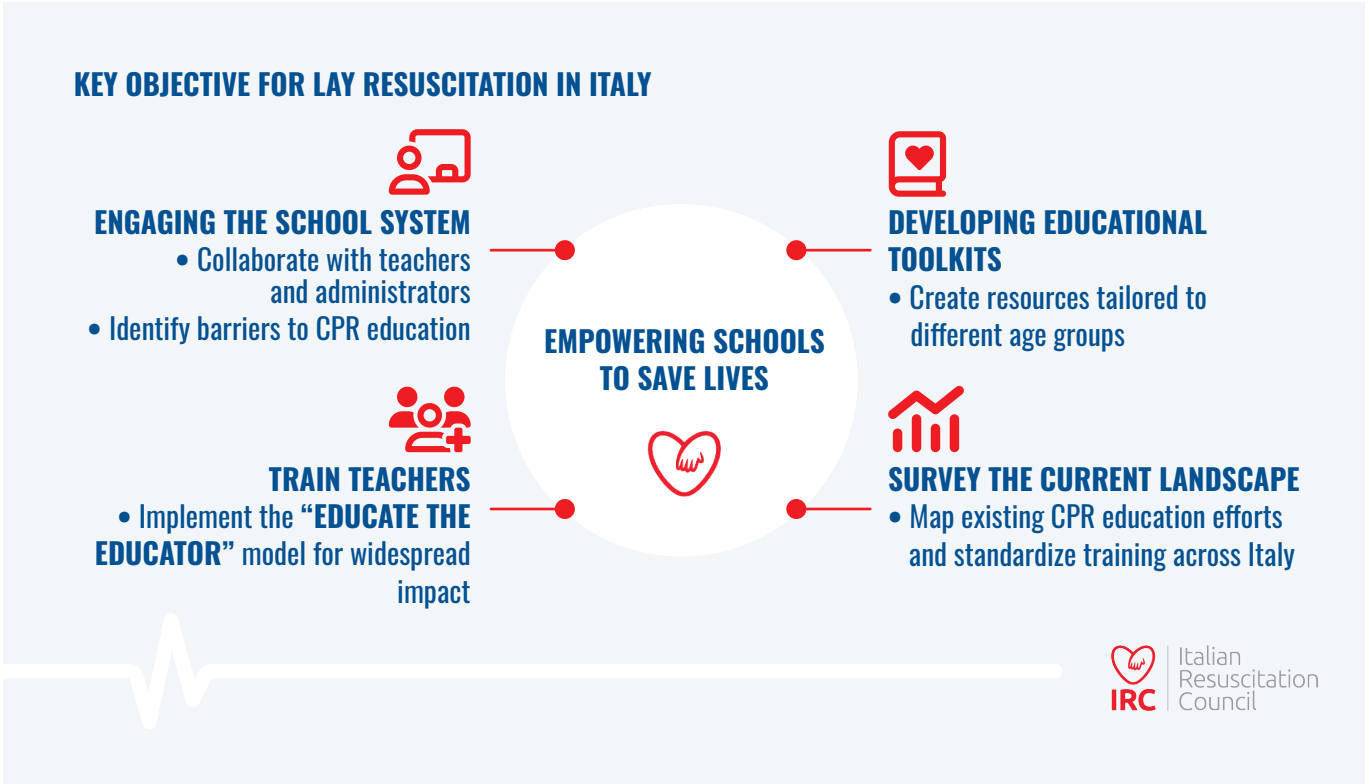
1. **Engaging the school system:** Develop strategies to reach teachers and students, emphasizing the importance of CPR while gathering insights into barriers and needs related to CPR education.
2. **Developing educational toolkits:** Design age-appropriate tools and resources to effectively communicate CPR concepts to various student age groups.
3. **Prioritizing teacher training:** Standardize CPR training for teachers to implement an "educate the educator" model, ensuring sustainability and widespread dissemination.
4. **Assessing the current landscape:** Conduct a comprehensive survey to map existing CPR education models across Italy, addressing the variability in the delivery of CPR training nationwide.

This initiatives aim to strengthen the first three links of the Chain of Survival and improve OHCA outcomes in Italy through widespread public awareness and training. Prioritizing school-based education, as highlighted in the *Kids Save Lives* manifesto, is seen as the most effective strategy to increase bystander CPR rates and foster a generational shift toward a CPR-aware society.[10]

The advisory board will establish a sustainable framework for CPR education, starting with the development of standardized training programs and age-appropriate toolkits for teachers and students. Key components of this initiative are expected to be in place by the 2024-2025 academic year, including a nationwide recognition of existing local educational program. Over time, the board aims to integrate CPR education into the national curriculum, ensuring consistency across Italy.

These efforts are expected to increase bystander CPR rates and improve OHCA survival. Progress will be monitored through IRC forthcoming Cardiac Arrest Registry, enabling the assessment of t raining outcomes and community impact.

FIGURE 1 - Key objective of advisory board for the Chain of Survival.



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STUDY PROTOCOL

Screening Tools for Patient Frailty in the Emergency and Urgent Care Setting: A Protocol for a Systematic Review

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Keywords: Drug Development; Drug Discovery; Drug Repositioning; Machine Learning; Artificial Intelligence.

Abstract

Background: Overcrowding in emergency departments (EDs) is a significant issue, leading to longer wait times and poor clinical outcomes, particularly affecting the elderly population. Elderly patients often visit EDs due to multiple chronic conditions and are at higher risk for hospitalization and adverse health outcomes. Frailty, an age-related condition characterized by increased vulnerability to health complications, plays a major role in this issue. Early identification of frailty can improve care and reduce ED congestion. Furthermore, boarding in the corridor, where patients, especially elderly ones, wait in hallways due to a lack of available beds, worsens overcrowding and impacts patient safety and care. **Aim:** This study aims to identify clinical scales for the rapid assessment of frailty in elderly patients, focusing on tools that can be integrated into daily ED workflows. Early frailty identification is key for improving clinical outcomes, reducing hospitalizations and mortality, and addressing the negative effects of corridor boarding. **Materials and Methods:** A systematic literature review was conducted to explore validated frailty scales suitable for emergency care settings. The PICO method was used to define the research question. Studies focusing on frailty assessment in aged patients admitted to Eds were analysed. A comprehensive search was conducted in PubMed, Embase, and Scopus with keywords like "frailty," "emergency department," and "screening." **Results:** Several frailty scales, including the Timed Up and Go (TUG), FRAIL Scale, and Clinical Frailty Scale (CFS), were identified

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as applicable in emergency settings. The Clinical Frailty Scale and Tilburg Frailty Indicator stood out for their simplicity and clinical utility. Boarding in the corridor was found to exacerbate the risks for frail patients, delaying care and leading to worse outcomes. **Conclusion:** Implementing a structured frailty screening system in EDs is essential to improve care, reduce hospitalizations, and address the challenges of overcrowding and corridor boarding.

Keywords: Frailty, Emergency Medical Services, Urgent Care, Geriatrics, Nurses, Aged

Introduction

Overcrowding in emergency departments (EDs) has become a major concern for healthcare facilities, resulting in longer wait times and poor clinical outcomes [1]. This issue, which affects public health and emergency care quality, has gained national attention, leading to urgent calls for reform [2]. The problem is compounded by the rising number of elderly patients, a significant portion of "frequent users" of emergency services. These patients, often seeking care for multiple chronic conditions, contribute to ED congestion [3]. Limited access to primary care and continuity of care are identified as key drivers of this issue. In Italy, individuals aged 65 and older represent about 20% of the population, with projections indicating that this will increase to 33.2% by 2050. Frequent ED users, who visit four or more times a year, are generally older and have a higher risk of hospitalization compared to younger patients [2,4]. The rise in chronic diseases, combined with increased frailty, contributes to the growing number of ED visits. The clinical needs of elderly patients presenting to EDs are substantially different from those of younger adults [5]. Many elderly patients suffer from acute or subacute illnesses, often accompanied by functional and/or cognitive decline. Additionally, these patients often have complex social care needs [6], requiring multidimensional assessments to improve care for this population, which indirectly benefits the entire population.

Frailty, a progressive decline associated with aging, increases vulnerability to stress and negative health outcomes [7]. The World Health Organization defines frailty as an age-related, multifactorial condition characterized by heightened vulnerability to adverse events and a reduction in intrinsic capacity, leading to a higher risk of hospitalization, disability, and death [8]. This decline in physiological reserves results in increased vulnerability to negative health effects such as falls, dependency, hospitalizations, and mortality [9].

Although physical frailty is widely studied, it also encompasses cognitive and psychosocial factors, which interact with each other and the external environment, defining frailty in specific contexts. Frailty differs from multimorbidity, the presence of multiple diseases, and disability, which refers to difficulties in performing daily activities. Fragile individuals often have multiple comorbidities that increase the risk of frailty and disability, creating a cycle of worsening health [7]. This complexity complicates the integration of frailty into clinical practice, as evidenced by the high number of severe triage codes in elderly patients, which heightens the risk of poor health outcomes in emergency situations [2].

Emergency care for the elderly requires more resources than for younger patients. Identifying frail elderly individuals and assessing their risk is crucial for providing appropriate care and guiding clinical decision-making [9] While frailty has a conceptual definition, an operational definition is needed to better identify and measure frailty in clinical settings [7].

Several models for assessing frailty exist, including the Phenotypic Model, the Deficit Model, and the Integrated Model [9]. The "Phenotypic Model" identifies frail individuals based on measurable physical capabilities such as weight loss, strength, fatigue, walking speed, and physical activity. While objective, it does not account for cognitive or social factors. The "Deficit Model" focuses on the number of health issues or diseases across various domains, including cognitive disorders, which are particularly relevant for the elderly. The "Integrated Model" adopts a comprehensive approach, incorporating social and psychological factors.

More functional tools, like the Clinical Frailty Scale, offer a simpler method for frailty assessment. This 9-step tool classifies frailty and functional impairments, aiding in risk stratification during emergency triage and directing patients to appropriate geriatric care. Other screening tools, such as the Geriatric Risk Profile and the Tilburg Frailty Indicator, also assist in early frailty identification and intervention

in emergency settings. Frailty and mobility assessment tools for the elderly include the Timed Up and Go (TUG) test, the FRAIL Scale, the Edmonton Frail Scale (EFS), and the Clinical Frailty Scale (CFS). The choice of tool depends on the context and objective, with some better suited for pre-frailty detection, while others predict long-term mortality. After identifying frail individuals, a comprehensive geriatric evaluation is advised to develop coordinated treatment and follow-up plans, considered the "gold standard" for frailty management.

Screening for cognitive decline, functional difficulties, and home care needs upon ED arrival is crucial to ensure appropriate care and guide discharge planning [2]. Elderly patients in the ED often present with both medical and social needs. Despite two-thirds of them being unable to perform at least one daily activity, functional and psychosocial decline is rarely recognized during emergency visits [10]. Patients with non-medical issues, such as social isolation, should be informed about community services. Case managers focusing on high-needs patients and providing structured follow-up can reduce ED visits and hospital admissions.

A more integrated healthcare system, with better monitoring for at-risk elderly individuals and prioritization of frailty assessment in care planning, is necessary to reduce ED overcrowding [11].

However, the main issue remains the lack of primary care facilities for post-acute care and tools that ensure continuity of care.

The COVID-19 pandemic highlighted the urgency of reforming the healthcare system, particularly the integration of hospital and community services. The strain on EDs during the pandemic, exacerbated by a surge in COVID-19 cases, has underscored the need for well-structured community-based care networks to reduce ED overcrowding and improve chronic disease and frailty management among the elderly.

In conclusion, the COVID-19 pandemic has emphasized the need for a healthcare system capable of preventing disease exacerbations and effectively managing resources at the community level. Prioritizing frailty identification and developing tools to screen elderly patients before ED visits will allow early detection and the application of appropriate territorial care strategies, improving overall healthcare quality and reducing ED congestion.

AIM

The aim of this study is to identify a valid and effective tool for the rapid identification of frail elderly patients upon admission to Emergency Departments (EDs). The study seeks to evaluate the effectiveness of various frailty scales in different clinical settings enabling targeted and personalized care planning, promoting the adoption of validated tools that can be used not only in Emergency Departments but also in community-based and pre-hospital services. Early identification of frailty in elderly patients is essential for improving clinical outcomes and reducing the risks associated with negative health consequences such as frequent hospitalizations, permanent disability, and increased mortality. Timely frailty assessment ensures that frail patients receive appropriate and personalized support based on their health status.

The study also aims to raise awareness among healthcare professionals about frailty as a critical factor in clinical decision-making, advocating for the development of more inclusive and preventive healthcare policies. Finally, this research aspires to contribute to the dissemination of scientific knowledge regarding the importance of early frailty identification and the adoption of clinical strategies tailored to meet the specific needs of this vulnerable population, with the goal of improving patient management and alleviating the phenomena of overcrowding and boarding in Emergency Departments.

METHODS

Study Design

Systematic Review The systematic review was not registered in PROSPERO because the authors opted to follow an alternative approach to protocol documentation and dissemination, such as publishing the protocol in a peer-reviewed journal. This decision was made to align with the review's specific objectives and the preferences of the research team **Search Strategy**

Authors performed the PICO method (see **Table 1**) to structure the research question (foreground question). This method relates four key elements: Population, Intervention, Comparison, and Outcome, in order to

identify a valid tool for the early identification of frail patients presenting to Emergency Departments (EDs).

P (Patient/Population) refers to geriatric patients over 75 years of age, who suffer from a complex clinical condition of "frailty" (insert reference), accessing emergency care and requiring multidisciplinary management.

I (Intervention) refers to the identification and use of validated scales for measuring frailty in the target population. These tools are already present in the literature and are used in international healthcare settings. Their application would allow for the early recognition of the patient's clinical condition, supporting healthcare providers.

C (Comparison) involves comparing the target population, for whom validated tools for early frailty identification are applied, with a group of patients for whom these scales are not used (control group). Through this comparison, the effectiveness of these scales in defining appropriate interventions can be assessed, with the aim of reducing inappropriate ED visits and the associated phenomena of overcrowding in healthcare facilities (e.g., boarding, aggression, etc.).

O (Outcome) refers to importance of implementing an effective screening tool for frail patients, particularly in Emergency Department settings, through the use of validated scales. This could lead to directing patients to alternative pathways such as outpatient follow-up programs, referrals to social and welfare services, home care, or rehabilitation facilities, thereby reducing the burden on emergency services. Additionally, it would support the development of personalized care plans, benefiting both patients and the multidisciplinary teams involved.
This approach aims to promote integrated and sustainable healthcare, addressing the specific needs of the elderly population. Moreover, these findings could contribute to the development of new guidelines for managing elderly patients in emergency settings, improving not only clinical outcomes but also the sustainability of the healthcare system. In conclusion, by using validated frailty scales, the goal is to enhance the management of elderly patients in the pre-hospital phase.

TABLE 1 - PICO Definition

P (Patient/Population)	Geriatric patients in the emergency-urgency context, with particular reference to emergency department settings.
I (Intervention)	Research and administration of validated scales defining the concept of frailty.
C (Comparison)	No administration of validated scales.
O (Outcome)	Screening fragile patients through the use of validated scales.

The project was structured in several phases:
- Definition of "key terms" and literature search for the most recent evidence regarding the presence of assessment scales for patient frailty.
- Selection of literature articles.
- Reading and analysis of the articles with the creation and use of a summary table.

To conduct the literature search, the databases PubMed, Embase, and Scopus were consulted using the key terms: *"frailty", "emergency department", "assessment", "scale", "score", "index", "hospital", "emergency care", "emergency service", "emergency ward", "emergency health service", "first aid department", "evaluation", "diagnostic scale", "screening"*.

The search string has been adapted to the Thesaurus of each consulted database for the investigation.

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Specifically, the search string included the use of the following terms and Boolean operators:

Inclusion and Exclusion Criteria

The studies to be included or excluded from the research were selected based on predefined eligibility criteria.
In particular, the inclusion criteria for the studies were:

- All studies related to the reference population: geriatric patients aged 75 years or older;
- All studies regarding scales/tools defining the concept of frailty;
- All studies related to the healthcare setting of Emergency and Urgency services and out-of-hospital settings (ER/118).

The exclusion criteria, on the other hand, included:

- All studies related to adult patients under 75 years of age;
- All studies referring to a population of oncology patients;
- All studies referring to a population of patients with a recent episode of trauma and/or related to orthopedic care;
- Studies referring to geriatric assessment including CGA (to be specified further);
- All articles dealing with tools/scales that do not concern the identification of frail patients.

Data extract and statistical analysis

Articles were identified through strings from Pubmed, Scopus and Embase. They were subsequently uploaded to RAYYAN software. The identified articles were extracted and entered into the portal through successive stages of: double-blind reading of the article titles and abstracts, was performed by two researchers, discarding those not relevant to the research; full-text reading, was performed by a researcherof the remaining articles and inclusion of those aligned with the research objective; resolving conflicts and analysing the articles.
The reserch strategy was report as a supplementary material.
The selected articles will be analysed through the development of a summary table to extract key information, including author, title, publication date, country of study, objective, research design, sample, interventions, type of training, type of evaluation, effectiveness of interventions, and outcomes.

Document Archiving

The Investigator is responsible for the archiving and storage of essential study documents before, during, and after the completion or termination of the study, in accordance with current regulations and GCP guidelines. The results of the study will be made available within 24 months of the conclusion of the systematic review through publication in an indexed scientific journal.

Expected results

The expected results of this study aim to identify an effective and reliable tool for the rapid identification of frail elderly patients upon their admission to Emergency Departments (EDs). By evaluating the effectiveness of different frailty scales in various clinical settings, the study seeks to determine which tools are most suitable for enabling targeted, personalized care planning. This could promote the adoption of validated frailty assessment tools not only within Emergency Departments but also in community-based and pre-hospital services.
Additionally, the study is expected to demonstrate how early identification of frailty in elderly patients can significantly improve clinical outcomes, reduce the risks associated with frequent hospitalizations, prevent permanent disabilities, and decrease mortality rates. The timely assessment of frailty is anticipated to ensure that frail patients receive appropriate, individualized care, tailored to their specific health needs.
Another key result is the increased awareness of healthcare professionals regarding frailty as a critical determinant in clinical decision-making. This study aims to advocate for the development of more inclusive and preventive healthcare policies that address frailty as a central component of care. Ultimately, the research aspires to contribute to the dissemination of scientific knowledge about frailty, encouraging the adoption of clinical strategies that are specifically designed to meet the needs of vulnerable elderly populations. The findings are expected to support improved patient management and help mitigate issues such as overcrowding and boarding in Emergency Departments.

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SUPPLEMENTARY MATERIAL: RESERCH STRATEGY

PUBMED:

(("Emergency Service, Hospital"[Mesh] AND "Frailty"[Mesh] AND ("Geriatric Assessment"[Mesh] OR "Physical Functional Performance")) OR(("Emergency Room*" OR "emergency department*" OR "ER" OR "Emergency Unit" OR "Emergency service*" OR "emergency ward*" OR "First Aid Department*" OR "emergency care" OR "Emergency Health Service*" OR "ED" OR "emergency admission*" OR "emergency clinic*") AND ("assessment*" OR "evaluation*" OR "scale*" OR "index" OR "scoring system*" OR "screening" OR "tool*" OR "diagnostic scale*") AND ("frail*"OR "fragilit*"))

SCOPUS:

('Emergency ward'/exp AND frailty/exp AND ('physical performance'/exp OR 'geriatric assessment'/exp)) OR (("Emergency Room*":ti,ab OR "emergency department*":ti,ab OR "ER":ti,ab OR "Emergency Unit":ti,ab OR "Emergency service*":ti,ab OR "emergency ward*":ti,ab OR "First Aid Department*":ti,ab OR "emergency care":ti,ab OR "Emergency Health Service*":ti,ab OR 'ED':ti,ab OR "emergency admission*":ti,ab OR "emergency clinic*":ti,ab) AND ("assessment*":ti,ab OR "evaluation*":ti,ab OR "scale*":ti,ab OR "index":ti,ab OR "scoring system*":ti,ab OR "screening":ti,ab OR "tool*":ti,ab OR "diagnostic scale*":ti,ab) AND ("frail*":ti,ab OR "fragilit*":ti,ab))

EMBASE:

(INDEXTERMS ("Emergency Service") AND INDEXTERMS ("Frailty") AND (INDEXTERMS ("Geriatric assessment") OR INDEXTERMS ("Physical functional performance"))) OR (TITLE-ABS ("Emergency Room*") OR (TITLE-ABS ("Emergency Room*") OR TITLE-ABS ("emergency department*") OR TITLE-ABS ("ER") OR TITLE-ABS ("Emergency Unit") OR TITLE-ABS ("Emergency service*") OR TITLE-ABS ("emergency ward*") OR TITLE-ABS ("First Aid Department*") OR TITLE-ABS ("emergency care") OR TITLE-ABS ("Emergency Health Service*") OR TITLE-ABS ("ED") OR TITLE-ABS ("emergency admission*") OR TITLE-ABS ("emergency clinic*"))AND (TITLE-ABS ("assessment*") OR TITLE-ABS ("evaluation*") OR TITLE-ABS ("scale*") OR TITLE-ABS ("index") OR TITLE-ABS ("scoring system*") OR TITLE-ABS ("screening") OR TITLE-ABS ("tool*") OR TITLE-ABS ("diagnostic scale*")) AND (TITLE-ABS ("frail*") OR TITLE-ABS ("fragilit*")))

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EDITORIAL

Mental health of university students through a pandemic event: what lessons did we learn?

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The COVID-19 pandemic severely affected our daily lives, bringing about significant changes that still permeate our society, encompassing the economic, social and scholastic spheres.
These effects had affected significantly the mental health of university students, as they had to navigate the challenges and uncertainties of daily life in the midst of a global crisis [1–12].
The implementation of strict measures such as lockdowns and social distancing guidelines resulted in major changes to their daily routines, causing a deep sense of loneliness and isolation [1,4,7–9,13,14]. The absence of face-to-face classes and limited social interactions, the lack of physical contact, restricted social gatherings, and limited opportunities for in-person connections left many students feeling disconnected from their peers and support networks, further exacerbating their mental distress [1,4,8]. Furthermore, with concerns about their financial stability and prospects students struggled to embrace their academic journeys while experiencing the difficulties of economic hardship [4,13].

To address these challenges, many institutions have implemented online psychological counseling services through their counseling centers [4,8,10,12]. By offering remote counseling sessions, students had access to professional help and guidance despite the physical limitations imposed by lockdowns [8]. These services played a vital role in providing support to students, as they were effective in alleviating distress, reducing feelings of isolation

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and providing a sense of continuity during these un precedented times [4,10,15]. In addition to individual counseling, universities have also organized online psychoeducational groups focusing on anxiety-management interventions, providing a safe context for students to interact with peers who share similar experiences and concerns [8], normalizing emotional struggles and fostering a collective understanding of the challenges faced during the pandemic. Recognizing the unique difficulties associated with remote learning, universities also organized online workshops on study methods aimed to address the specific challenges encountered with online learning, such as maintaining motivation, managing time effectively, and overcoming the absence of in-person interaction and immediate feedback from teachers [8]. All these adopted measures could be interpreted as a signal that scholastic environments are becoming more receptive to the mental wellbeing of their students.

As we approach the post-pandemic phase, academic institutions are resuming their activities, welcoming back university students. In the future it could be tempting to discard all the implemented measures, but we shouldn't discard all the positive initiatives that have been implemented since 2020. Indeed, several pre-pandemic studies reported that university students struggled with mental health well before the COVID-19 pandemic [16-18], highlighting the necessity to increase the offer of psychological support throughout their academic journey. Furthermore, the profound changes experienced during the pandemic took a toll on the mental health of students that could possibly persist for a long period, making it necessary to provide further support in the next years. Indeed, online interventions have the potential to reduce the mental health burden experienced by students, increasing the interest to further explore their potential as a daily tool [19-22].

With the surge in interest in student's mental health during the pandemic brought to the development and implementation of innovative tools, the efforts toward a supportive academic environment should not be discontinued in the future, instead it could be beneficial to further potentiate them.

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LETTER TO EDITOR AND EXPERT COMMENTARY

Ranolazine for cardiac arrest: moving from *ex vivo* studies to clinical relevant *in vivo* models

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After successful cardiopulmonary resuscitation (CPR), approximately 70% of patients die prior to hospital discharge, mainly due to post-resuscitation myocardial and cerebral dysfunction [1]. Premature ventricular beats and life-threatening episodes of ventricular tachycardia and ventricular fibrillation (VF) commonly occur during the early minutes after resuscitation. Furthermore, an overall condition of severe myocardial dysfunction, including variable degrees of systolic and diastolic impairment, is present. Among the mechanisms underlying early post-resuscitation arrhythmia and myocardial dysfunction, cytosolic and mitochondrial calcium (Ca2+) overload have been recognized as a pivotal factor [2].

In a landmark randomized placebo-controlled trial, the Ranolazine Implantable Cardioverter-Defibrillator (RAID) published on JACC Clin Electrophysiol, Younis et al. [3] demonstrated that ranolazine, a drug commonly prescribed for the treatment of chronic stable angina pectoris, reduces the recurrence of ventricular tachycardia (VT) requiring implantable cardioverter-defibrillator (ICD) therapy. A study involving 1,012 patients identified seven factors associated with increased VT burden, including age ≥65 years, history of VT, and atrial fibrillation. Ranolazine significantly reduced VT burden in patients not on concomitant anti-arrhythmic drugs and those with cardiac resynchronization therapy ICDs [3]. This effect was elegantly explained as an improved dysregulation of intracellular Ca2+ accomplished by ranolazine through the sodium (Na+) current inhibition during VF. Based on these results, the potential therapeutic use of ranolazine

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in the setting of cardiac arrest (CA) is suggested, and testing in specific in vivo models is advocated.

We also support the potential role of ranolazine in improving the outcome of VF in terms of successful termination of the malignant arrhythmia and post-resuscitation myocardial dysfunction by blocking the Na+-dependent intracellular Ca2+ overload [4]. Starting from this hypothesis, in 2015 we investigated the effects of ranolazine in a rat model of VF, demonstrating for the first time that this drug was able to improve CA outcomes [5]. Indeed, ranolazine significantly improved defibrillation outcome, assessed by amplitude spectrum area, and reduced of almost 60% early post-resuscitation arrhythmias with hemodynamic instability. Finally, ranolazine significantly improved both post-resuscitation left ventricle (LV) systolic and diastolic dysfunction and survival. Despite these enthusiastic results, the potential of ranolazine as a future therapeutic option for CA remains to be determined. In fact, in our study, the drug was administered as a pretreatment, i.e. before the induction of VF [5]. This approach was selected to ensure ranolazine delivery to the myocardium before circulatory arrest; however, it limited the extrapolation of results to the clinical setting. We are now performing new studies with the same rat model of CA but with a more clinically relevant design, including the administration of ranolazine after resuscitation. Surprisingly, the preliminary results disagree with the earlier benefits observed with the pretreatment, showing an abruptly increased mortality when ranolazine is administered early after resuscitation. A severe hypotension, not observed in the instance of pretreatment, seems to be the most likely cause of such deaths.

Thus, further studies are needed to prove ranolazine's real benefits and elucidate the mechanisms of cardioprotection and potential adverse effects, as recently observed by our group. For these reasons, the clinical application of ranolazine in the treatment of VF cardiac arrest is still far away.

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LETTER TO EDITOR AND EXPERT COMMENTARY

Mental health of university students through a pandemic event: what lessons did we learn?

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The COVID-19 pandemic severely affected our daily lives, bringing about significant changes that still permeate our society, encompassing the economic, social, and scholastic spheres. These effects had significantly affected the mental health of university students, as they had to navigate the challenges and uncertainties of daily life in the midst of a global crisis [1-3]. The implementation of strict measures such as lockdowns and social distancing guidelines resulted in major changes to their daily routines, causing a deep sense of loneliness and isolation [1-4]. The absence of face-to-face classes and limited social interactions, the lack of physical contact, restricted social gatherings, and limited opportunities for in-person connections left many students feeling disconnected from their peers and support networks, further exacerbating their mental distress [1,2]. Furthermore, with concerns about their financial stability and prospects students struggled to embrace their academic journeys while experiencing the difficulties of economic hardship [1,4].

To address these challenges, many institutions have implemented online psychological counseling services through their counseling centers [1,2]. By offering remote counseling sessions, students had access to professional help and guidance despite the physical limitations imposed by lockdowns [2]. These services played a vital role in providing support to students, as they were effective in alleviating distress, reducing feelings of isolation and providing a sense of continuity during these unprecedented times [1]. In addition to individual counseling, universities have also organized online

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psychoeducational groups focusing on anxiety-management interventions, providing a safe context for students to interact with peers who share similar experiences and concerns [2], normalizing emotional struggles and fostering a collective understanding of the challenges faced during the pandemic. Recognizing the unique difficulties associated with remote learning, universities also organized online workshops on study methods aimed to address the specific challenges encountered with online learning, such as maintaining motivation, managing time effectively, and overcoming the absence of in-person interaction and immediate feedback from teachers [2]. All these adopted measures could be interpreted as a signal that scholastic environments are becoming more receptive to the mental wellbeing of their students.

As we approach the post-pandemic phase, academic institutions are resuming their activities, welcoming back university students. In the future it could be tempting to discard all the implemented measures, but we shouldn't discard all the positive initiatives that have been implemented since 2020. Furthermore, the profound changes experienced during the pandemic took a toll on the mental health of students that could possibly persist for a long period, making it necessary to provide further support in the next years. Indeed, online interventions have the potential to reduce the mental health burden experienced by students, increasing the interest to further explore their potential as a daily tool [5].

With the surge in interest in student's mental health during the pandemic brought to the development and implementation of innovative tools, the efforts toward a supportive academic environment should not be discontinued in the future, instead it could be beneficial to further potentiate them.

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