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Original Article

# Accuracy of preoperative lung ultrasound score for the prediction of major adverse cardiac events in elderly patients undergoing HIP surgery under spinal anesthesia: The LUSHIP multicenter observational prospective study

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ABSTRACT

*Background and objective:* We hypothesize that lung ultrasound scores (LUS) can help stratify the cardiac risk of elderly patients undergoing orthopedic surgery for hip fracture, adding value to the Revised Cardiac Risk Index (RCRI), the American Society of Anesthesiologists Physical Status (ASA-PS) and the National Surgical Quality Improvement Program Myocardial infarction and Cardiac arrest (NSQIP-MICA).
*Methods:* Prospective, observational multicenter study of 11 Italian hospitals on patients aged >65 years with hip fractures needing urgent surgery. Subjects with major adverse cardiovascular events (MACE) in the previous 6 months or with ongoing acute heart failure were excluded. Trained anesthesiologists obtained preoperative LUS scores during preoperative evaluation. ROC curve analysis and comparison were used to evaluate test accuracy.
*Results:* A total of 877 patients were enrolled in the study period. 108 MACE events occurred in 98 patients, with an overall incidence of 11.2%. LUS score was higher in complicated than non-complicated patients, $11.6 \pm 6.64$ *vs.* $4.97 \pm 4.90$ ($p < 0.001$). Preoperative LUS score ≥8 showed both better AUC (0.78) and accuracy (0.76) in predicting MACE than the RCRI scores ($p < 0.001$), MICA scores ($p = 0.001$) and ASA classes ($p < 0.001$). LUS sensitivity was 0.71, specificity was 0.76, negative predictive value was 0.95. LUS score ≥8 showed an OR for MACE of 5.81[95% CI 3.55–9.69] at multivariate analysis. 91 patients (10.4%) experienced postoperative pneumonia showing a preoperative LUS score higher in the non-pneumonia group, $p < 0.001$.
*Conclusions:* The preoperative LUS score, with its high negative predictive value, could improve patients' risk stratification when used alone or add further value to the RCRI score.
*Registration:* Registered at clinicaltrials.gov as NCT04074876.


## 1. Introduction

With more than 10 million cases per year globally, hip fracture is one of the most common orthopedic surgical procedures in elderly patients [1,2]. The incidence of complications reported after this surgery appears to be between 22% and 53% [3], despite the European Society of Cardiology (ESC) and the European Society of Anesthesiology (ESA) guidelines placing hip surgery at an intermediate level of cardiac risk [4,5]. Anesthesiologists are therefore called to assess the preoperative risk and to take the necessary steps to improve the outcome of this increasing population of patients [6,7]. Classical scoring systems such as the American Society of Anesthesiologists Physical Status (ASA-PS) [8], the Revised Cardiac Risk Index (RCRI) [9], and the National Surgical Quality Improvement Program Myocardial infarction and Cardiac arrest (NSQIP-MICA) [10] seem to work only moderately well and do not sufficiently predict either overall cardiac events or overall mortality [11,12]. This might reflect in an ineffective allocation of these surgical patients to the appropriate level of postoperative monitoring. In addition, the recent MET-repair study has revealed that evaluating self-reported metabolic equivalents (METs) did not improve the predictive accuracy of RCRI risk scores, nor did their association with the use of the natriuretic peptides (NT-proBNP and BNP) [13,14]. On the other hand, investigation for implementing ultrasound techniques into perioperative diagnostic pathways has been highly recommended, as recent studies showed [15,16]. In particular, some reports have highlighted the role of lung ultrasound (LUS) in combination with high-sensitivity troponins as a guide for clinicians to identify vascular patients at increased risk for myocardial injury after noncardiac surgery (MINS) [17]. Although B-lines are not specific of cardiac or pulmonary disease, there is a well-recognized cut-off to define the diffuse interstitial syndrome, and both lung [18] and focused cardiac ultrasound (FoCUS) have been demonstrated to help differentiate the etiology [19,20]. This syndrome may reflect a pre-clinical condition of pulmonary congestion due to fragile cardiopulmonary pathophysiology, that is frequent in older patients. In line with this, the American College of Physicians (ACP) recommends that all patients with hip fractures undergo a risk assessment that focuses also on chronic obstructive pulmonary disease (COPD) and congestive heart failure [21]. Therefore, this study aimed to investigate the role of LUS in the preoperative evaluation of such patients, hypothesizing that preoperative LUS, assessed as LUS score, can be used for the stratification of cardiac risk in elderly patients undergoing hip fracture under spinal anesthesia, possibly adding value to the classical scoring systems.

## 2. Methods

### 2.1. Study setting and design

LUSHIP was a prospective observational multicenter study performed in 11 Italian university and non-university centers. The study was approved by the Ethics Committee of Friuli Venezia Giulia (CEUR-FVG) with the identification number #2817 on June 4$^{th}$, 2019 (with LV as the principal investigator). On August 30$^{th}$, 2019, the study was registered at clinicaltrials.gov as NCT04074876. Study enrolment was planned to occur from September 2019 to September 2020 or until the calculated sample size was reached. The study protocol was described in depth in a previous publication [22]. The study followed the Standards for the Reporting of Diagnostic Accuracy Studies (STARD) for Point-of-Care Ultrasound (POCUS) [23,24].

### 2.2. Patients' characteristics

Patient inclusion criteria were age >65 years, entering the emergency department (ED) for hip fracture needing urgent surgery (<24 hours), under spinal anesthesia, and the willingness to participate in the study. Exclusion criteria were inability to obtain informed consent, the need for general anesthesia, acute heart failure at the time of preoperative evaluation, major adverse

cardiovascular events (MACE) in the previous 6 months, history of preexisting pulmonary pathologies (known history of pulmonary fibrosis, chronic renal failure on dialysis, fibrothorax, recent pneumothorax, and patients with previous lobectomy or pneumonectomy) and positive COVID-19 assay from either nasal or pharyngeal swabs during the pandemic surge. Patients were planned to be enrolled based on the availability of the local investigators. The choice to limit the investigation to spinal anesthesia patients was taken to reduce any confounding due to postoperative pulmonary complications.

### 2.3. Study protocol for lung ultrasound

The LUS score is based on recognizing four aeration patterns and is calculated by assigning a value ranging between 0 and 3 to each of the six defined areas of both lungs. These areas are identified using the anterior and posterior axillary lines as vertical boundaries for the anterior, lateral, and posterior faces of the lungs, further divided into superior and inferior areas, bringing the count to six areas for each side. On each of the twelve areas, the local pattern is evaluated within the worst scan of the single area, and points are assigned. The possible patterns are i) the absence of B-lines, or their presence to a maximum of two (0 points); ii) three or more B-lines occupying at maximum 50% of the pleural line (1 point); iii) B-lines occupying more than 50% of the pleural line, to a condition of coalescent B-lines (2 points); iv) any subpleural consolidation with at least 10 mm of length at the pleural level (3 points). Given this, the total LUS score is the sum of the twelve local points and can range from 0 to 36. Multiple variations to this score have been proposed, but the Authors decided to keep this definition. To improve inter-operator agreement, an online site initiation visit was performed among the principal investigators of each study center, under the supervision of EBo, using a preselected sample of video clips with a specific focus on LUS score evaluation. LUS was always performed before surgery, if possible, at the same time as the preoperative anesthesiologic evaluation. Strict boundaries about the timing of ultrasound evaluation from the hospital access and blinding of the results were judged as unfeasible. LUS assessment was carried out by the principal investigator (PI) of each study center, or from local experts under investigator supervision. Each study center was allowed to use the ultrasound machines available considering the hospital's internal resources. Finally, we also compared the performance of the diffused interstitial syndrome (DIS), which corresponds to the presence of at least two areas with at least 1 point both on the right and left side of the patient.

### 2.4. Reference tests

The ASA class was assigned to every patient during the anesthesiologic evaluation according to the American Society of Anesthesiologists (ASA) definitions. The RCRI and NSQIP-MICA were calculated as soon as laboratory results were available, according to their definitions.

### 2.5. Endpoints

The primary endpoint of this study was to evaluate whether a systematic preoperative LUS examination can provide better accuracy in the postoperative prediction of major advanced cardiac events occurrence than the classical preoperative scoring system, the ASA-PS, the RCRI, and NSQIP-MICA.

The secondary endpoints were i) to evaluate if preoperative LUS combined with the classical preoperative scoring system can improve their prediction accuracy for MACEs, and ii) to identify a possible association between the LUS score before surgery and postoperative pneumonia, this last according to the standards for definitions and use of outcome measures in perioperative medicine by the European Society of Anaesthesiology and Intensive Care (ESAIC) and the European Society of Intensive Care Medicine (ESICM) [25].

### 2.6. Data collection and follow-up

Patients were followed in the postoperative period to assess clinical deterioration suspected of MACE. Evaluation of the events was left to the physicians in charge of the patients during the 30-day follow-up phase through electronic medical record surveys, telephone contacts, or post-discharge outpatient assessments, depending on the local organization.

Among the relevant major advanced cardiac events already described in the literature [26], we decided to focus on the new onset of atrial fibrillation requiring cardiologist consultation, the development of heart failure, acute myocardial infarction, or cardiac arrest as for our previous study [27]. We also collected data about postoperative pneumonia and mortality at the same time point. A website, LUSHIP. it., was created to guarantee a homogenous and safe data gathering, preventing missing data, and providing shared key documents and information about study protocol.

### 2.7. Patient consent and data protection

Patients were informed about the study, and written consent was requested. If the patient could not write their signature, verbal consent was asked for in the presence of two witnesses. The data were processed according to the Declaration of Helsinki and the European Privacy Regulation 2016/679 for the General Data Protection Regulation (GDPR). In each center, the PI was responsible for their institution's data collection, ensuring proper concealment of patient identity on the linked CRF and storing links between sensitive data and patient univocal codes under appropriate protection. During the study period, two independent investigators (FL and EBo) performed the data quality assessment, checking for abnormalities and inconsistencies among reported data. More importantly, implementing the study did not alter the patient's management during or following surgery.

### 2.8. Statistical analysis

Continuous normally distributed variables were presented as means ± standard deviations (SD) and compared using the student's t-test. Normality was assessed using the Shapiro–Wilk test and visual inspection of quantile-quantile plots. Non-normally distributed data were presented as medians and 1$^{st}$ and 3$^{rd}$ quartiles and compared using the Wilcoxon rank-sum test. Categorical data were compared between groups using the $\chi^2$ or Fisher's exact test. Possible correlations between the patient outcomes and changes in LUS score were examined using Spearman's rank correlation coefficient. Receiver-operating characteristic (ROC) curve analysis was used to determine the optimal cutoff values of LUS for the aims of detecting the development of any MACE and the development of postoperative pneumonia. Similarly, the ROC curve was used to determine the existence of cutoff values for the reference tests in predicting MACEs, before comparing them. Youden's index calculation defined the best cutoff value. Logistic models for MACE as endpoints were employed to calculate odds ratios (OR) and their corresponding 95% confidence intervals (95% CI) of LUS parameters. The selection of variables for inclusion in the model was conducted using an automated approach based on the Akaike Information Criteria (AIC) [28]. Due to the substantial number of covariates, a genetic algorithm was implemented to systematically explore the candidate set of models,

optimizing the selection process for robust predictive performance. The center effect was evaluated using the intraclass correlation coefficient (ICC) estimated from a random-effects model and was excluded if found to be non-significant. Concordance between predicted and observed outcomes was assessed using Somer's Dxy Index (where values closer to 1 in absolute terms indicate better performance), and prediction accuracy was measured by the Brier score (where values closer to 0 indicate better alignment with actual outcomes). Both metrics were derived using 50 bootstrap replications through the function "validate" [29]. Statistical analysis was performed using the R version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria). *P*-values less than 0.05 were considered to indicate statistical significance.

### 2.9. Sample size calculation

Considering a conservative scenario with the rate of MACE in patients undergoing hip surgery at approximately 10%, a sample size of 877 patients would achieve 87% power to detect a difference of 8% between a diagnostic test area under the ROC curve (AUC) of 0.70 and another diagnostic test with an AUC of 0.78 using a two-sided z-test.

## 3. Results

### 3.1. Patients' characteristics and enrollment

From September 3, 2019, to September 21, 2022, 1,677 patients were identified as undergoing hip fracture procedures. Of these, 937 (55.87%) were finally enrolled in the study. For switching to general anesthesia, protocol violation, and a single case of death between enrollment and surgery, 877 patients were finally available for analysis (Fig. 1). Overall, the recruitment phase took 36 months (1,109 days), with enrollment slowing during the COVID-19 pandemic. Supplementary Fig. S1 shows a detail of the trimestral performance of the 11 centers.

The median patient age was 83 years (IQR 75–89). Female gender was prevalent (73.2%). Median BMI was 24.4 $Kg.m^{-2}$ (IQR 22–27.3). According to declared functional status, 49.1% were autonomous, 37.6% were partially dependent, and 13.3% were dependent on daily living activities. Table 1 reports a detailed analysis of sample characteristics and comorbidities.

### 3.2. MACE and reference scoring systems

A total of 108 MACE occurred in 98 patients, with an overall MACE incidence of 11.2%. In detail, 52 patients developed a new onset of atrial fibrillation (5.9%), 49 patients underwent acute heart failure (5.6%), and two patients presented acute myocardial infarction (0.2%). Five patients suffered in-hospital cardiac arrests (0.6%). Death occurred in 4 cases, and the crude mortality was 0.46%. Of note, dividing the study into 6 periods of 6 months each, MACE occurrence was significantly reduced during the five COVID-19 periods compared to the first (Supplementary Fig. S2).

Stratification of the LUS score for each value of the three primarily used scoring systems ASA, RCRI, and MICA is reported in Table 2. Among all risk scores examined, only RCRI $> 2$ demonstrated a significant association with MACE compared to the ASA class and MICA score (OR 2.32[95% CI 1.76–3.08], $p < 0.001$).

### 3.3. LUS score and MACE

LUS score sample distribution showed a median value of 4 (IQR 1–8). Patients who developed MACE in the postoperative period showed a mean LUS score of 11.6 (SD 6.64 [95% CI 10.27–12.93]), compared with no-MACE patients, who exhibited a lower mean LUS score of 4.97 (SD 4.90 [95% CI 4.62–5.31], $p < 0.001$). LUS scores showed a progressive increase among the different classes of the other 3 predictors ($p < 0.001$) (Supplementary Fig. S3).

At ROC curve analysis, a LUS threshold of 7.5 points was identified. Dichotomizing LUS score into negative (range 0–7, 625 patients) and positive (range 8–36, 252 patients) this test was characterized by a sensitivity of 71.43%, a specificity of 76.64%, a

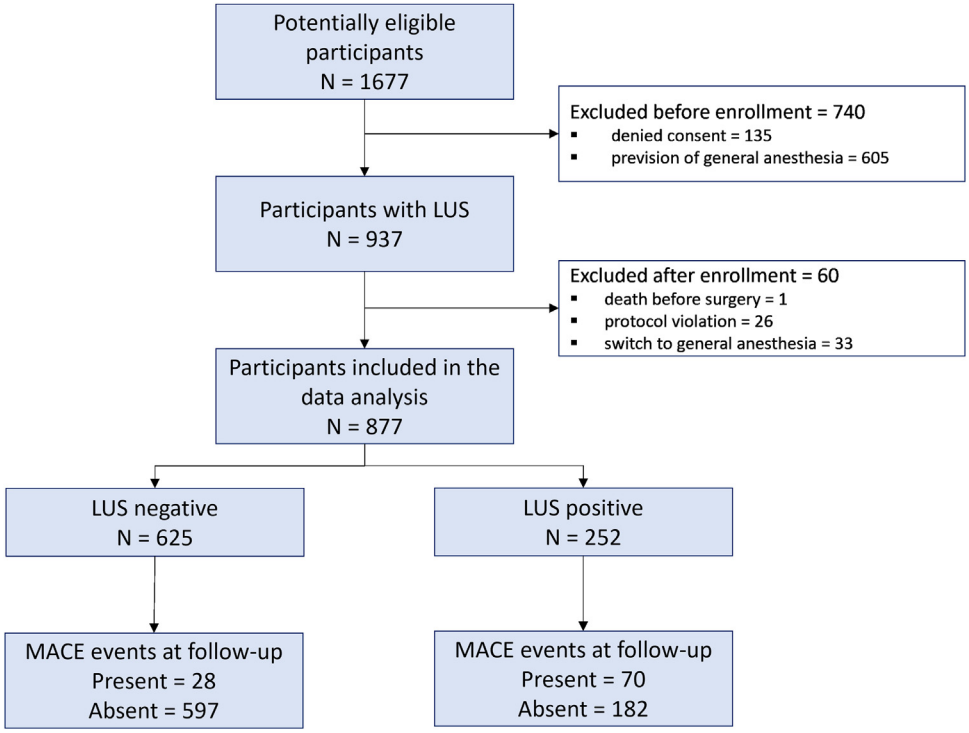


**Fig. 1.** Study flow chart.

**Table 1**
Baseline characteristics of included patients.

| General anthropometric values | Overall N = 877 | MACE N = 98 | Non-MACE N = 779 |
|---|---|---|---|
| Age classes, n (%) | | | |
| 65–69 | 83 (9.5) | 12 (12.2) | 71 (9.1) |
| 70–74 | 100 (11.4) | 5 (5.1) | 95 (12.2) |
| 75–79 | 124 (14.1) | 15 (15.3) | 109 (14) |
| 80–84 | 181 (20.6) | 22 (22.4) | 159 (20.4) |
| 85–89 | 208 (23.7) | 23 (23.5) | 185 (23.7) |
| 90–94 | 128 (14.6) | 13 (13.3) | 115 (14.8) |
| 95+ | 53 (6.0) | 8 (8.2) | 45 (5.8) |
| Male gender, N (%) | 235 (26.8) | 27 (27.6) | 570 (73.2) |
| BMI, median [IQR] | 24.4 [22–27.3] | 24.7 [22.4–27.7] | 24.2 [21.7–27.3] |
| Smoking habit, N (%)) | | | |
| Past | 203 (23.1) | 19 (19.4) | 184 (23.6) |
| None | 563 (64.2) | 61 (62.2) | 502 (64.4) |
| Active | 111 (12.7) | 18 (18.4) | 93 (11.9) |
| Medical History, N (%) | | | |
| CAD | 140 (16.0) | 31 (22.1) | 109 (77.9) |
| CHF | 94 (10.5) | 32 (34) | 62 (66) |
| Stroke | 101 (11.5) | 16 (15.8) | 85 (84.2) |
| Diabetes mellitus | 109 (12.4) | 21 (19.3) | 88 (80.7) |
| CKD (sCr >1.5 mg/dl) | 121 (13.8) | 32 (26.4) | 89 (73.6) |
| CKD (sCr >2.0 mg/dl) | 38 (4.3) | 12 (31.6) | 26 (68.4) |
| Hypertension | 160 (18.2) | 18 (11.3) | 142 (88.8) |
| ECG rhythm, N (%) | | | |
| Sinusal rhythm | 728 (83.0) | 77 (78.6) | 651 (83.6) |
| AF/atrial flutter | 136 (15.5) | 21 (21.4) | 115 (14.8) |
| Pacemaker | 11 (1.3) | 0 (0) | 11 (1.4) |
| Other | 2 (0.2) | 0 (0) | 2 (0.3) |
| Functional status, N (%) | | | |
| Independent | 430 (49.1) | 40 (40.8) | 390 (50.1) |
| Partially dependent | 330 (37.6) | 38 (38.8) | 292 (37.5) |
| Totally dependent | 117 (13.3) | 20 (20.4) | 97 (12.5) |
| Daytime hospital access, N (%) | 615 (70.1) | 62 (63.3) | 553 (71.0) |
| Time to LUS, median [IQR] | 27 [16.0–50.7] | 29.7 [10.6–68.5] | 26.7 [16.2–49.2] |
| Access to OR, N (%) | | | |
| Weekdays | 730 (83.2) | 81 (82.7) | 649 (83.3) |
| Weekends | 147 (16.8) | 17 (17.3) | 130 (16.7) |
| Time to surgery, median [IQR] | 39.4 [22–65.2] | 42.6 [23–75.7] | 39.2 [21.6–64.2] |

BMI, body mass index; CAD, coronary artery disease; CHF, chronic heart failure; CKD, chronic kidney disease; OR, operating room.

**Table 3**
ROC curve analysis of lung ultrasound (LUS) score, American Society of Anesthesiologists (ASA) classes, Revised Cardiac Risk Index (RCRI) score, and Myocardial Infarction and Cardiac Arrest (MICA) score in predicting major adverse cardiac events occurrence.

| | Threshold | Sensitivity | Specificity | PPV | NPV | Accuracy | 95% CI | *p*-value |
|---|---|---|---|---|---|---|---|---|
| LUS | 7.50 | 0.71 | 0.77 | 0.27 | 0.96 | 0.76 | 0.73–0.84 | |
| ASA | 2.50 | 0.79 | 0.43 | 0.15 | 0.94 | 0.47 | 0.57–0.67 | <0.001 |
| RCRI | 0.50 | 0.68 | 0.62 | 0.18 | 0.94 | 0.69 | 0.63–0.74 | <0.01 |
| MICA | 1.05 | 0.67 | 0.56 | 0.16 | 0.93 | 0.57 | 0.58–0.69 | <0.001 |

ASA, American Society of Anesthesiologists score; RCRI, Revised Cardiac Risk Index score; MICA, Gupta Perioperative Risk for Myocardial Infarction or Cardiac Arrest; LUS, lung ultrasound score; PPV, positive predictive value; NPV, negative predictive value.

positive predictive value of 27.78%, and a negative predictive value of 95.52%. When the ROC curves comparison between ASA, RCRI, and MICA *vs.* LUS score to predict MACE occurrence was carried out, accuracy comparison showed overlapping results with AUROC comparison. LUS score had better accuracy (0.76) in predicting MACE occurrence than the RCRI score (0.69, $p < 0.01$), MICA score (0.57, $p < 0.001$), and ASA classes (0.47, $p < 0.001$) (Table 3). The ROC curve areas were 0.78, 0.69 ($p < 0.001$), 0.63 ($p < 0.001$), and 0.62 ($p < 0.001$), respectively (Fig. 2).

### 3.4. Univariate and multivariate analysis

The results of the logistic model for MACE are presented in Table 4. After selecting them in the univariate analysis based on their statistical significance, clinically significant variables were included in the model. The LUS score ≥8, the history of congestive heart failure, and a value of creatinine >1.5 mg/dL were found to be independent predictors of developing MACE. In particular, LUS score ≥8 has an adjusted OR of 5.81 [95% CI 3.55–9.69], CHF history 3.29[1.85–5.79], and creatinine 2.08[1.19–3.58]. In more detail, a 16% increase in OR for MACE is associated with every 1-point increment in LUS score (adjusted OR 1.16[1.12–1.21].

To verify the influence of the different centers participating in the study, we also built a model incorporating the center as a random effect. Intraclass correlation coefficient (ICC) explained no

**Table 2**
Major adverse cardiovascular events (MACE) rate according to different risk stratification scores and the relative distribution of lung ultrasound score within them.

| ASA physical status | N, (%) | LUS score, median [IQR] | Overall MACE incidence[§], N (%) | Atrial fibrillation, N (%) | Acute heart failure, N (%) | Acute myocardial infarction, N (%) | Cardiac arrest, N (%) |
|---|---|---|---|---|---|---|---|
| 1 | 10 (1.1) | 0.50 [0.00, 4.00] | - | - | - | - | - |
| 2 | 349 (39.8) | 3.00 [0.00, 6.00] | 20 (5.7) | 15 (4.3) | 9 (2.6) | - | - |
| 3 | 464 (52.9) | 6.00 [2.00, 10.00] | 69 (14.9) | 37 (8.0) | 33 (7.1) | 1 (0.2) | 5 (1.1) |
| 4 | 54 (6.2) | 8.00 [3.00, 14.00] | 9 (16.7) | 1 (1.9) | 7 (13.0) | 1 (1.9) | 1 (1.9) |
| RCRI score | | | | | | | |
| 0 | 513 (58.5) | 3.00 [1.00, 7.00] | 31 (6.0) | 17 (3.3) | 16 (3.1) | - | 2 (0.4) |
| 1 | 264 (30.1) | 4.00 [2.00, 8.00] | 33 (12.5) | 17 (6.4) | 18 (6.8) | - | 2 (0.8) |
| 2 | 83 (9.5) | 8.00 [4.00, 14.00] | 25 (30.1) | 13 (15.7) | 10 (12.0) | 2 (2.4) | 1 (1.2) |
| 3 | 15 (1.7) | 13.00 [6.25, 18.00] | 7 (46.7) | 6 (40.0) | 3 (20.0) | - | - |
| 4 | 2 (0.2) | 18.00* | 2 (100) | - | 2 (100) | - | - |
| MICA classes | | | | | | | |
| 1 | 660 (75.3) | 3.00 [1.00, 7.00] | 66 (10) | 43 (6.5) | 28 (4.2) | 2 (0.4) | 3 (0.5) |
| 2 | 156 (17.8) | 6.00 [2.00, 10.00] | 17 (10.9) | 9 (5.8) | 8 (5.1) | - | 1 (0.6) |
| 3 | 40 (4.6) | 7.50 [4.00, 12.00] | 10 (25) | 1 (2.5) | 8 (20) | - | 1 (2.5) |
| 4 | 21 (2.4) | 12.00 [7.00, 16.25] | 5 (23.8) | - | 5 (23.8) | - | - |

ASA, American Society of Anesthesiologists score; RCRI, Revised Cardiac Risk Index score; MICA, Gupta Perioperative Risk for Myocardial Infarction or Cardiac Arrest; LUS, lung ultrasound score; MACE, major adverse cardiovascular events.

* RCRI level 4 IQR not reported.

§ Overall MACE incidence was calculated as the percentage of patients with at least one MACE over the patient at risk in the single stratum according to the scoring system. Atrial fibrillation and other events percentage are calculated as events over the patients at risk.

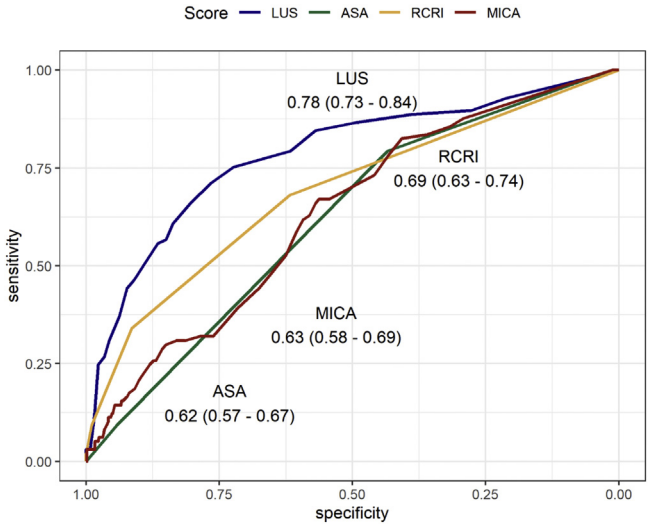


**Fig. 2.** ROC curve comparison, with AUROC and 95% CI values of LUS score, ASA classes, RCRI score, and MICA score in predicting MACE occurrence. ASA, American Society of Anesthesiologists score; RCRI, Revised Cardiac Risk Index score; MICA, Gupta Perioperative Risk for Myocardial Infarction or Cardiac Arrest; LUS, lung ultrasound score; MACE, major adverse cardiovascular events.

more than 9% of the total variance, suggesting a minimal impact from center-related factors.

### 3.5. Secondary endpoint

Regarding the secondary outcome, 91 patients (10.4%) experienced postoperative pneumonia and showed a LUS score of 9.5 (SD 7.3) *vs.* 5.3 (SD 5.1) in the non-pneumonia group, $p < 0.001$. For the prediction of postoperative pneumonia, the ROC curve analysis (Supplementary Fig. S4) identified a LUS score threshold of 7 (negative group, range 0–6, 588 patients; positive group, range 7–36, 289 patients), and AUROC of 0.67, a sensibility of 62.64%[51.87–72.56] and specificity of 70.48% [67.16–73.65].

## 4. Discussion

### 4.1. Primary endpoint

According to our knowledge, this is the first study to use preoperative lung ultrasound (LUS) to assess such a large cohort of elderly patients undergoing hip fracture under spinal anesthesia. In our population, 11.2% (98 out of 877) of patients experienced MACE. They were not sufficiently risk-stratified by the classical ASA, MICA, and RCRI scores which demonstrated a moderate predictive ability performance.

Whereas a preoperative LUS score $\geq 8$ showed an AUROC of 0.78 and better accuracy in risk stratification. In particular, its strong negative predictive value (NPV) of 0.95 allows the identification of low-risk patients.

### 4.2. LUS integration in preoperative assessment

RCRI demonstrated a better prediction for MACE. Using this result to generate a hypothesis, we speculated whether the incorporation of the dichotomized LUS score into the RCRI increased the accuracy of the latter in MACE prediction or not. Using the thresholds identified at ROC analysis, the use of the LUS score to help classify as low-risk more patients within those who already have a high RCRI score, raised the accuracy of the RCRI from 69% (95% CI 0.63–0.74) to 79% (95% CI 0.74–0.85) with $R^2$ increasing from 0.12 to 0.26 (Brier Score improving from 0.09 to 0.08). On the other hand, a dichotomous LUS score alone (with its sound adjusted OR of 5.81 for MACE when LUS $> 8$) might also be used alongside a history of heart failure (adjusted OR 3.29) and serum creatinine >1.5 mg/dL (adjusted OR 2.08) into a clinical risk assessment tool to obtain a more nuanced evaluation of a patient's perioperative risk.

**Table 4**
Multivariate analysis of the risk associated with main predictors of major adverse cardiovascular events (MACE).

| Predictors | Adjusted OR | 95% CI | *p*-value |
|---|---|---|---|
| CHF | 3.29 | 1.85–5.79 | <0.001 |
| Stroke | 1.55 | 0.79–2.92 | 0.182 |
| ASA | 1.07 | 0.70–1.63 | 0.760 |
| sCr >1 5 mg/dL | 2.08 | 1.19–3.58 | 0.009 |
| LUS (dichotomous) | 5.81 | 3.55–9.69 | <0.001 |
| Observations | 877 | | |
| $R^2$ Tjur | 0.175 | | |

CHF, chronic heart failure; ASA, American Society of Anesthesiologists score; sCr, serum creatinine; LUS, lung ultrasound score; $R^2$ Tjur, Coefficient of Discrimination.

Hip fracture patients should undergo surgery as soon as possible since this is associated with better outcomes and reduced healthcare costs [30–32]. However, this may conflict with the time needed for eventual preoperative optimization to reduce perioperative risk [32]. In the context of an aging global population, the incidence of hip fractures is expected to rise, increasing the urgency for reliable preoperative risk assessment tools [1,2,33]. To assess risk, there are currently four scoring systems in use. In general, the ASA score works well for identifying low-risk patients, but less well in those at high risk [12]. The RCRI score works moderately well for cardiovascular risk estimation (*i.e.*, cardiac death, myocardial infarction, and nonfatal cardiac arrest), but less well in predicting noncardiac mortality [11]. According to the literature, the performance of NSQIP-MICA is better than the ASA score for assessing the risk associated with overall 30-day complications, but it is not specific for cardiac events prediction [11,12].

Moreover, evidence from a MET-repair study demonstrated that MET estimation yielded no improvement in prediction accuracy of postoperative cardiac events compared with clinical risk factors only, and this also remained true for natriuretic peptides (NPs) in a sub-study with over 3,600 patients [13,14].

In other words, determination of METs or NPs plasma levels did not improve the RCRI score prediction of cardiac events that are reported in the literature in a wide range, between 0.5% and 30% of cases, carrying increased postoperative morbidity and mortality risk [34,35].

Few studies on preoperative LUS as a screening tool exist. Gillmann *et al.*, in a prospective single-center observational study, reported using lung ultrasound to distinguish patients at increased risk for myocardial injury after noncardiac surgery (MINS) [17]. The authors showed that increased B-lines were associated with elevated MINS incidence.

Notwithstanding, we should be aware that a recent study with 700 patients undergoing a preoperative cardiologist consultation before noncardiac and nonvascular surgery did not demonstrate reduced MACE occurrence [36]. As a consequence, a cardiology consultation before intermediate-risk surgical procedures, including hip fracture, would not have a direct impact on preoperative management or outcome [37,38].

In the context of hip fracture, the role of point-of-care ultrasound is a matter of debate, with controversial results in the literature [39,40].

Our study contributes to this goal by demonstrating that LUS, with its higher NPV, can identify patients who are less likely to experience MACE, thus facilitating timely surgical interventions

without unnecessary delay and, eventually, indicating which patients may need more optimization and more intensive postoperative monitoring [41–43].

Collateral advantages of a point-of-care LUS approach during the preoperative phase afford more than the speed and reliability of such a bedside exam since its use might reduce exposure to ionizing radiation, contributing to greener anesthesia and reduced diagnostic costs[41,44].

### 4.3. Secondary endpoint

Regarding postoperative pneumonia, the ability of the preoperative LUS score to predict this condition was only moderate (AUC 0.67, $p < 0.001$).

On this topic, Boussier *et al.* recently studied the ability of the LUS score, assessed before surgery and on postoperative days 1, 4, and 7, to predict postoperative pulmonary complications (PPC) [16]. They found an AUROC of 0.65 for predicting postoperative pulmonary complications before day 10, with a LUS score cutoff greater than 12, which showed a sensitivity of 0.54, specificity of 0.77, and negative predictive value of 0.74.

Zieleskiewicz *et al.* and Dransart-Rayé *et al.* evaluated early LUS evaluation after extubation in major surgical patients and highlighted how the detection of immediate postoperative alveolar consolidation and pleural effusion is associated with postoperative pulmonary complications and morbimortality [45,46].

Likewise, B-lines, as a sign of increased extravascular lung water, were significantly correlated with a new onset of preclinical and pre-radiological acute congestive heart failure with a B-line cutoff $\geq$15 [47]. On the other hand, the absence of multiple bilateral B-lines excludes cardiogenic pulmonary edema with a negative predictive value close to 100% [43,48,49].

We have wondered if classifying our patients according to the definition of diffuse interstitial syndrome (DIS) from the International Evidence-Based Recommendations for Point-of-Care Lung Ultrasound, which mostly means a LUS $\geq$ 4, may accurately predict MACE occurrence. It turned out that the presence of DIS was associated with higher MACE occurrence (chi-square 67.95, $p < 0.00001$) and predicted a higher MACE risk (RR 5.14 [3.31–7.97], $p < 0.001$).

### 4.4. Limitations

This study has some limitations and these need to be highlighted. Firstly, the widespread application of LUS is not without challenges. The successful implementation of LUS requires adequate training to achieve consistency and accuracy in ultrasound interpretation. The results of our study may have been influenced by the high proficiency of the researchers participating in LUS execution, suggesting that a standardized training program and certification in LUS would be beneficial for broader application. Secondly, B-lines are not specific and not always related to cardiac congestion, especially during the 2019–2020 period and COVID-19 crisis. This emphasizes the need for comprehensive clinical correlation and possibly adjunctive diagnostic tools to discern the etiology of the observed ultrasound findings; these were not assessed in our investigation.

Third, even though described in our published protocol in terms of timing and definitions, the detection of the occurrence of major adverse cardiovascular events was left to the investigators' assessment and therefore may have suffered some grade of underreporting [22]. Fourth, this study focused only on patients treated with spinal anesthesia as a methodological choice of the authors to avoid a possible source of confounding from general anesthesia and mechanical ventilation. This might reduce the generalizability of our results. However, in a recently published meta-analysis, Zhou *et al.* showed that there were no differences in mortality between general and regional anesthesia management for elderly patients with hip fracture and we are confident that the effects of this choice are negligible [50]. Lastly, the LUS evaluation has been carried out at different times from emergency department access to surgical intervention. The timing of LUS has been evaluated as a covariate in the multivariate and has not been found significant, so we are confident that this item has not been a source of confounding. Moreover, the intraclass correlation coefficient (ICC) explained no more than 9% of the total variance, suggesting in our study a minimal impact from center-related factors, disputing that ultrasound is necessarily an operator-dependent exam.

### 4.5. Implications for research

To further establish the utility and applicability of LUS, future studies should aim to externally validate these findings in different populations and investigate the effects of I LUS training on the accuracy of risk stratification. Additionally, understanding the full spectrum of conditions associated with B-lines in LUS will be crucial for accurately interpreting and applying this diagnostic modality in perioperative medicine.

## 5. Conclusions

In conclusion, our research suggests LUS as a potential preoperative assessment tool, enhancing the accuracy of cardiac risk prediction and supporting timely surgical interventions without contributing to delays. As the world's aging population is predicted to create a surge in the demand for hip fracture interventions, the role of LUS could become increasingly pivotal in better identifying low-risk patients.

#### Human and animal rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans as well as in accordance with the EU Directive 2010/63/EU for animal experiments.

#### Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s).

The authors declare that they obtained a written informed consent from the patients and/or volunteers included in the article. The authors also confirm that the personal details of the patients and/or volunteers have been removed.

#### Disclosure of interest

The authors declare that they have no known competing financial or personal relationships that could be viewed as influencing the work reported in this paper.

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Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.accpm.2024.101432.

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