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ORIGINAL ARTICLE

Development and validation of a score to predict postoperative respiratory failure in a multicentre European cohort

A prospective, observational study

Jaume Canet, Sergi Sabaté, Valentín Mazo, Lluís Gallart, Marcelo Gama de Abreu, Javier Belda, Olivier Langeron, Andreas Hoeft, Paolo Pelosi, For the PERISCOPE group*

BACKGROUND Postoperative respiratory failure (PRF) is the most frequent respiratory complication following surgery.

OBJECTIVE The objective of this study was to build a clinically useful predictive model for the development of PRF.

DESIGN A prospective observational study of a multicentre cohort.

SETTING Sixty-three hospitals across Europe.

PATIENTS Patients undergoing any surgical procedure under general or regional anaesthesia during 7-day recruitment periods.

MAIN OUTCOME MEASURES Development of PRF within 5 days of surgery. PRF was defined by a partial pressure of oxygen in arterial blood (PaO_2) less than 8 kPa or new onset oxyhaemoglobin saturation measured by pulse oximetry (SpO_2) less than 90% whilst breathing room air that required conventional oxygen therapy, noninvasive or invasive mechanical ventilation.

RESULTS PRF developed in 224 patients (4.2% of the 5384 patients studied). In-hospital mortality [95% confidence interval (95% CI)] was higher in patients who developed PRF [10.3% (6.3 to 14.3) vs. 0.4% (0.2 to 0.6)]. Regression modelling identified a predictive PRF score that includes seven independent risk factors: low preoperative SpO_2; at least one preoperative respiratory symptom; preoperative chronic liver disease; history of congestive heart failure; open intrathoracic or upper abdominal surgery; surgical procedure lasting at least 2 h; and emergency surgery. The area under the receiver operating characteristic curve (*c*-statistic) was 0.82 (95% CI 0.79 to 0.85) and the Hosmer–Lemeshow goodness-of-fit statistic was 7.08 ($P = 0.253$).

CONCLUSION A risk score based on seven objective, easily assessed factors was able to predict which patients would develop PRF. The score could potentially facilitate preoperative risk assessment and management and provide a basis for testing interventions to improve outcomes.
The study was registered at ClinicalTrials.gov (identifier NCT01346709).

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From the Department of Anaesthesiology and Postoperative Care Unit, Hospital Universitari Germans Trias i Pujol (JC, VM), Department of Anaesthesiology, Fundació, Puigvert (SS), Department of Anaesthesiology, Hospital del Mar, IMIM (Institut Hospital del Mar d' Investigacions Mèdiques), Universitat Autònoma de Barcelona, Barcelona, Spain (LG), Department of Anaesthesiology and Intensive Care Medicine, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany (MGDA), Department of Anaesthesia and Critical Care, Hospital Clínico Universitario, University of Valencia, Valencia, Spain (JB), Department of Anaesthesiology and Critical Care, Université, Pierre et Marie Curie-Paris VI, CHU Pitié-Salpêtrière, Paris, France (OL), Department of Anaesthesiology and Intensive Care Medicine, University of Bonn, Bonn, Germany (AH), and Department of Surgical Sciences and Integrated Diagnostics, IRCCS San Martino Hospital-IST, University of Genoa, Genoa, Italy (PP)

Correspondence to Jaume Canet, Department of Anaesthesiology and Postoperative Care Unit, Hospital Universitari Germans Trias i Pujol, Badalona, 08916 Barcelona, Spain
Tel: +34690953029; fax: +34934978749; e-mail: jcanet.germanstrias@gencat.cat
* Members of the PERISCOPE (Prospective Evaluation of a RIsk Score for postoperative pulmonary COmPlications in Europe) group are listed in the Appendix.

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Introduction

Postoperative respiratory failure (PRF) is the most frequent postoperative pulmonary complication (PPC) and has a major impact on outcome and health costs.[1–7] The pathogenesis of PRF depends on factors related to patient status as well as anaesthetic and surgical procedure.[8–10] The incidence of PRF in general surgical populations ranges between 0.2 and 3.4%[8] and several scoring systems for predicting PRF have been proposed.[1,3–7,11] However, previous studies developing scores to predict PRF have defined this complication in different ways. Definitions that have been used include unexpected tracheal reintubation,[1,5,7,11] the need for postoperative mechanical ventilation[1,3] or postoperative acute lung injury (ALI) and acute respiratory distress syndrome (ARDS).[4,6] In addition, the majority of the available scoring systems have been developed from retrospective databases that contain administrative information and coding.[1,3,5–7,11] Retrospectively identified predictors have certain limitations,[12–15] including low positive predictive values and moderate reliability, and they are subject to errors in data collection, higher percentages of missing values and the lack of information on variables of clinical interest.

Current thinking on the diagnosis of PRF calls for the use of objective measures of newly developing hypoxaemia detected during the postoperative course,[8] specifically a partial pressure of oxygen in arterial blood (PaO_2) less than 8 kPa (60 mmHg), which usually corresponds to an arterial oxygen saturation less than 90%. Furthermore, according to the most recent international consensus on ARDS, the severity of PRF may be further classified as mild, moderate or severe based on the ratio of PaO_2 to the inspiratory oxygen fraction (FIO_2).[16] Stratifying risk for different degrees of PRF severity could potentially facilitate the early detection and management of this complication.

In this study, we used a large European database of general surgical cases (PERISCOPE cohort – Prospective Evaluation of a RIsk Score for postoperative pulmonary COmPlications in Europe)[17] that had been created to externally validate the ARISCAT risk score[2] for a PPC composite. Hypothesising that it would be possible to use the PERISCOPE data to build a simple risk score to predict PRF alone, we designed the present secondary analysis. Our aims were to identify perioperative risk factors for PRF and build and internally validate a specific predictive model. We also stratified PRF at three levels of severity on the basis of the presence of hypoxaemia and type of respiratory support in order to assess differences in outcome.

Materials and methods

Study design

A cohort of surgical patients was created for the observational multicentre PERISCOPE study. Sixty-three European hospitals (Appendix) recruited patients during continuous 7-day periods, choosing a convenient date to begin data collection between 2 May and 15 August 2011. Follow-up ended in November 2011. The participating hospitals constituted a convenience sample of volunteer centres found through the European Society of Anaesthesiology (ESA). Candidates were approached directly by national study coordinators. The study was registered at ClinicalTrials.gov (identifier NCT01346709).

PERISCOPE cohort inclusion and exclusion criteria

Consecutive patients undergoing in-hospital elective or emergency surgery under general (including combined general anaesthesia) or regional (neuroaxial or plexus block) anaesthesia were recruited.

Exclusion criteria were as follows: age under 18 years; obstetric procedures or any procedure during pregnancy; procedures in which only local or peripheral nerve anaesthesia would be used; procedures outside an operating theatre; procedures related to a previous postoperative complication; organ transplantation; patients who had undergone tracheal intubation preoperatively; and outpatient procedures, defined as those requiring a hospital stay less than 24 h.

Ethical considerations

Ethical requirements differed in the 21 countries, but formal approval from a research ethics review board was applied for and given in each. The locally responsible investigator applied for and obtained approval from the ethics committee of each participating hospital. Written informed consent was obtained from each patient.

Organisation, data collection and quality assurance

The research team consisted of a steering committee in addition to nationally and locally responsible investigators, who were all anaesthesiologists. Data collectors, who did not modify a centre's customary management of patients, used a structured questionnaire to record the following information: administrative data [dates of surgery and discharge; status (alive or dead) at discharge], general information (sex, date of birth date, height and weight), preoperative variables [oxyhaemoglobin saturation measured by pulse oximetry (SpO_2) breathing air in supine position after 1 min resting breathing air, or in patients on oxygen, SpO_2 after 10 min without oxygen]; respiratory symptoms based on a simplified version of the Medical Research Council questionnaire;[18] respiratory infection in the last month; haemoglobin concentration; cough test; chronic pulmonary disease; smoking status; American Society of Anesthesiologists ASA class; and intraoperative variables [surgical incision, surgical duration in hours, type of surgery (scheduled or emergent), description of procedure, surgical specialty and anaesthetic technique]. Definitions of all variables can be found in the online supplement (Supplementary Table 1, http://links.lww.com/EJA/A65).

The data collectors also sought all PPCs by searching medical records daily to find relevant events until hospital discharge; information on PRF was, therefore, recorded, as this complication developed throughout the hospital stay. Data were collected on paper forms and then transferred anonymously to secure online case records (OpenClinica, Boston, Massachusetts, USA). This electronic system incorporated quality control algorithms to validate online data entry and identify missing data. An off-site data manager checked entries to confirm completeness and asked the local team contact to provide additional information if necessary. An expert on the International Classification of Diseases (Ninth Revision, Clinical Modification) coded all diagnoses and procedures at the end of the collection period.

Outcomes

The primary outcome of interest for this secondary analysis was PRF, which was defined as new-onset hypoxaemia appearing within 5 postoperative days at three levels of severity: mild (PaO_2 <8 kPa or SpO_2 <90% on room air but responding to mask/nasal supplemental oxygen); moderate (necessitating noninvasive or invasive mechanical ventilation to treat a PaO_2 <8 kPa or SpO_2 <90%); or severe [requiring invasive mechanical ventilation to manage a PaO_2/FiO_2 <26.7 kPa (200 mmHg) regardless of the level of positive end-expiratory pressure (PEEP)]. Hypoventilation and heart failure were excluded in all cases. Hypoventilation considered likely to be due to residual effects of anaesthetics or opiates was evaluated clinically by the investigators, and heart failure was defined as signs of diffuse alveolar interstitial infiltrates with dyspnoea and rates related to left ventricular failure confirmed by one of the following: echocardiography; pulmonary artery catheter monitoring; or clinical improvement with specific treatment.

Secondary outcomes of interest were postoperative ICU admission, postoperative length of stay (LOS) and in-hospital mortality.

Statistical analysis

The size of the PERISCOPE cohort had been calculated to provide at least 10 events per variable that we expected to enter into the logistic regression model.[19] It was estimated that the 63 PERISCOPE centres would be able to collect around 5000 cases and that the incidence of PRF would be around 3%.[1,2,20,21] Recording at least 150 PRF events would allow around 15 predictor variables to be entered into logistic regression. Demographic and clinical characteristics are expressed in percentages and median (interquartile range, IQR).

Potential PRF predictors were selected according to the investigators' consensus on measurable preoperative variables or the results of previous studies.[2,22] Independent continuous variables (age, SpO_2 and duration of surgery) were grouped into categories on the basis of the investigators' understanding of relevant clinical cut points.

To compare patients with and without PRF, all categorical variables were analysed with the Chi-square test or the Fisher exact test, as appropriate, for associations with the outcome. Bivariate odds ratios (ORs) and 95% confidence intervals (95% CIs) were also estimated. The possibility of colinearity between categorical variables was tested with the Cramer V test (nominal variables) or Kendall's tau-b (ordinal variables).

The logistic regression model was constructed using a backward stepwise selection procedure in which the presence of PRF was the dependent variable. Independent predictors were entered into the model if a significant association ($P < 0.05$) was identified on bivariate analysis and the correlation coefficient between them (colinearity) was less than 0.25. Potential predictors were removed if this exclusion did not result in a significant change in the log-likelihood ratio test. The cut-off for variable removal was set at a significance level of 0.05. Adjusted ORs and 95% CIs were also calculated.

To avoid overfitting and to obtain reliable internal validation of the subset of factors, we used a bootstrap method,[23] deriving 1000 computer-generated samples by random selection with replacement, each including the same number of patients. Within each bootstrap sample, the β coefficient was calculated using all selected independent variables. The robustness of the model and, thus, the reliability of predictor variables in the final regression model were estimated by the 95% CI of the β coefficient derived from the bootstrap samples.

A simplified predictive risk score for clinical use was then calculated by multiplying each β coefficient (corrected after bootstrapping) by 10 and rounding to the nearest integer. The integers were added together to produce an overall PRF risk score for each patient. To evaluate the ability of the score to predict increasing PRF risk, we used the minimum description length principle[24] to divide the sample into three risk levels, each with a similar number of patients. The logistic regression model's calibration was then assessed by the Hosmer–Lemeshow goodness-of-fit statistic and by plotting the actual frequency of PRF in each of the three risk levels against the predicted probability of PRF in that risk group.

To assess the ability of the simplified PRF risk score to discriminate between patients with and without PRF, we used the *c*-statistic, which was also displayed graphically as the area under the receiver operating characteristic (ROC) curve. In addition, to check the performance of the model if it were used without information for any single factor such as SpO_2 (which might not be recorded in all centres), we also checked the discriminative performance by calculating the *c*-statistics and calibration statistics for alternative six-factor models.

The Mann–Whitney *U* test was used to compare postoperative LOS between patients with and without PRF. An actuarial life table was constructed to assess in-hospital mortality after development of mild, moderate or severe PRF. The Wilcoxon–Gehan test was used to compare overall survival curves.

Statistical analyses were performed using the SPSS software package (version 20.0; IBM Corp., Armonk, New York, USA). Bootstrapping was performed using R, version 3.0.2 (R Project for Statistical Computing).

Results

Of 5859 initially eligible patients, 5384 (91.9%) were included in the final analysis (Fig. 1). The characteristics of patients and procedures are detailed in Table 1.

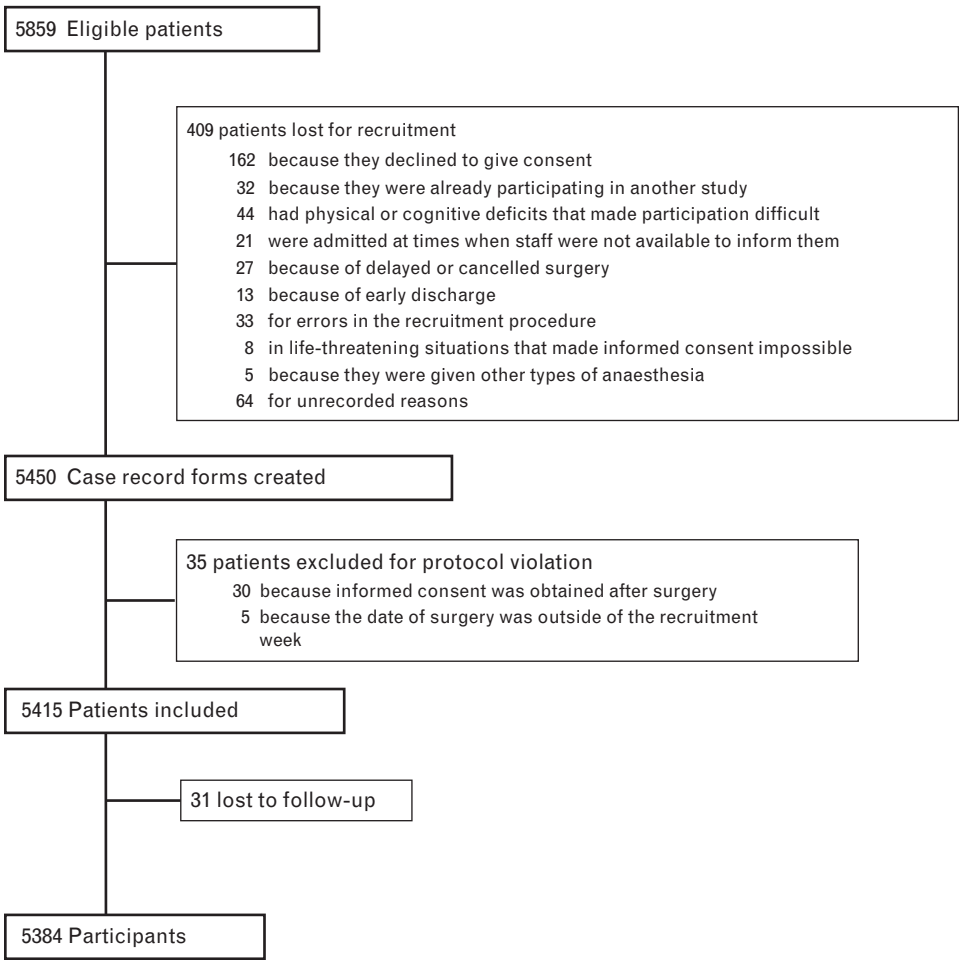
PRF developed in 224 patients (4.2% of the cohort) and was classified as mild in 155 (2.9%), moderate in 43 (0.8%) and severe in 26 (0.5%). The time between surgery and the onset of PRF was a median of 0.5 days (0 to 1). In 54.9% of the patients with PRF, symptoms began within 24 h and in 94.6% onset was within 3 days.

Postoperative respiratory failure, ICU stay, postoperative length of stay and mortality

Intensive care admission was required in 181 (80.8%) of the patients who developed PRF and in 318 (6.2%) of the patients who did not. The ICU stay was significantly longer in patients who developed PRF ($P < 0.001$). These patients were in the ICU a median of 44 (24 to 96.5) h, whereas the median stay for patients without PRF was 22 (12 to 46) h.

The median in-hospital postoperative stay was also longer in patients with PRF [9 (5 to 14) vs. 4 (2 to 7) days] ($P < 0.001$). Forty-six patients died in the hospital; 23 of them had PRF (10.3% of the 224 patients with PRF) and 23 did not (0.44% of the 5160 without PRF) ($P < 0.001$). Figure 2 shows survival curves for in-hospital mortality according to PRF severity. Differences in

Fig. 1



Recruitment flowchart.

Table 1 Demographic and clinical characteristics of patients

Total number of patients	5384 (100)
Male sex	2733 (50.8)
Age (years)	58.9 (44.7 to 70.7)
Smoking status	
Never smoked	2833 (52.6)
Former smoker	1309 (24.3)
Current smoker	1242 (23.1)
Preoperative SpO_2 (%)	97 (96 to 99)
BMI ($kg\,m^{-2}$)	26.1 (23.4 to 29.4)
COPD	538 (10.0)
Respiratory infection in the last month	298 (5.5)
ASA physical status	
1	1204 (22.4)
2	2738 (50.8)
3	1336 (24.8)
4	106 (2.0)
Emergency surgery	609 (11.3)
Anaesthesia	
General and combined[a]	4125 (76.6)
Neuraxial/Regional	1259 (23.4)
Surgical specialty	
General and digestive	1427 (26.5)
Orthopaedic	1064 (19.8)
Urology	702 (13.0)
Gynaecology	452 (8.4)
Neurosurgery	333 (6.2)
Ear, nose and throat	322 (6.0)
Vascular	211 (3.9)
Cardiac	167 (3.1)
Breast	161 (3.0)
Thoracic	145 (2.7)
Other	400 (7.4)
Duration of surgery (h)	1.3 (0.8 to 2.2)
Preoperative length of stay (days)	1 (0 to 1)
Postoperative ICU admission	499 (9.3)
ICU length of stay (h)	24 (12 to 67)
Postoperative hospital length of stay (days)	4 (2 to 7)
In-hospital mortality	46 (0.9)

Data are number (%) of patients or median (IQR) as appropriate. ASA, American Society of Anesthesiologists physical status classification; COPD, chronic obstructive pulmonary disease; SpO_2, oxyhaemoglobin saturation by pulse oximetry breathing air in supine position. [a]This category included general anaesthesia alone and general anaesthesia combined with regional blockade.

hospital mortality between PRF severity levels were statistically significant ($P < 0.001$).

Risk factors and postoperative respiratory failure score

The independent variables entered into logistic regression are summarised in Table 2, along with variables that were not significant on bivariate analysis or that were significant but rejected because of high colinearity with other variables. Multivariable logistic regression selected seven independent predictors of PRF, four were related to the patient's presurgical health status (low preoperative SpO_2 breathing air, respiratory symptoms, heart failure and chronic liver disease) and three were procedure-related (open thoracic or abdominal surgery, duration of surgery, and emergency surgery). All were retained in more than 95% of the bootstrap subsamples. Table 3 summarises the ORs for these predictors. The seven-variable regression model had good discrimination (*c*-statistic 0.82) and calibration (Hosmer–Lemeshow, $P = 0.253$). The area under the ROC curve (*c*-statistic) and the calibration plot are presented in Fig. 3. Supplementary Table 2, http://links.lww.com/EJA/A65 shows the statistics reflecting the performance of the model without inclusion of preoperative SpO_2 or any other single factor; the *c*-statistic fell to 0.81 for that model and all other alternative six-variable models created by removing one of the factors.

The incidence of PRF increased significantly between risk levels (low <12 points; intermediate 12 to 22 points; and high ≥23 points). The incidences (95% CIs) were 1.1% (0.7 to 1.5), 4.6% (3.4 to 5.6) and 18.8% (15.8 to 21.8), respectively, for each level. Table 4 summarises sensitivity, specificity and other statistics assessing the predictive utility of the cut-offs for moderate risk (≥ 12 points) and high risk (≥ 23 points).

Discussion

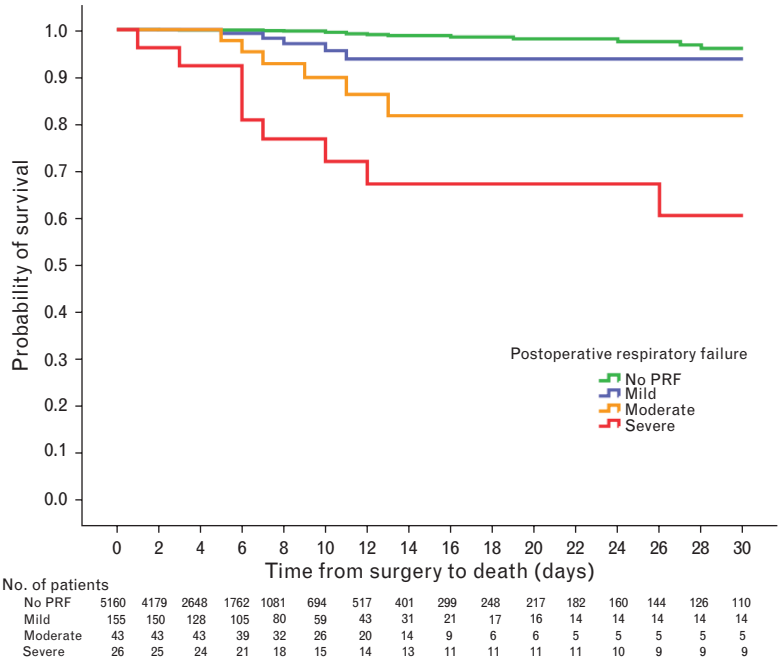
The incidence of PRF in this prospective, multicentre surgical cohort receiving general or regional anaesthesia was 4.2% and the risk of developing PRF was predicted by a score based on seven easily recorded predictors. The PERISCOPE-PRF score performed well, as it was able to identify 82% of the patients who would develop PRF (as shown by the *c*-statistic of 0.82) and it was able to distinguish three levels of risk. Calibration measures showed good agreement between the predicted and observed values within the risk levels; bootstrapping confirmed the stability of the dataset and all seven predictors were retained after the procedure. PRF significantly increased the ICU admission rate, postoperative LOS and in-hospital mortality.

Several studies of risk have defined a composite PPC as the primary outcome.[2,22,25,26] The complications most often included are respiratory infection, bronchospasm, PRF, atelectasis and pleural effusion. Although such an approach to risk modelling is useful for guiding preoperative management and vigilance, clinicians are aware that the pathogenesis and clinical impact of each component in the composite is substantially different. We therefore designed the present study to determine whether the PERISCOPE model, also designed to predict a composite, could be used to predict only PRF.

Most previous studies of PRF defined this complication as the need for more than 48 h of mechanical ventilation or unplanned reintubation,[1,3,5,7,11] which would only identify the most severe forms of PRF. The predictive scores for PRF developed in these studies showed *c*-statistics ranging from 0.79[11] to 0.89[3]. The *c*-statistic of 0.82 for the PERISCOPE-PRF score fell within this range and is consistent with those earlier findings in spite of differences in definitions or study design.

The incidence of PRF in this cohort (4.2%) was higher than previous rates, which ranged from 2.6 to 3.4%.[1,8,20] There are important methodological, population and outcome definition differences between our study and

Fig. 2



Plot of survival predicted by the risk score against overall (actuarial) survival after development of mild, moderate or severe postoperative respiratory failure. PRF, postoperative respiratory failure.

the earlier ones that can account for the higher rate. Our definition of PRF specified that new-onset hypoxaemia of noncardiac cause must have appeared within 5 postoperative days, marked objectively by a level of SpO_2 less than 90% breathing air, which corresponds approximately to a PaO_2/FIO_2 of less than 40 kPa (300 mmHg). There is no consensus about the postoperative period within which a pulmonary complication can be considered attributable to surgery.[8] Several studies analysed PRF developing within 30 days,[1,3,11] whereas others limited the time frame to 3 to 7 days.[4–7] We chose a 5-day period so that the complication and the surgical/anaesthetic events would be clearly linked, thereby excluding 8.9% of the PERISCOPE patients who later developed this complication. Although we included patients without previous lung injury and lacked information to calculate the PaO_2/FIO_2 for all patients, we did classify PRF in three levels of severity, in a way that was similar to the recent ARDS classification.[16] Our stratification was based on the presence of hypoxaemia and the kind of respiratory support required to manage it (conventional oxygen therapy and noninvasive or invasive mechanical ventilation regardless of PEEP level), a classification consistent with current clinical management of PRF. Up to 74% of these patients can be managed with noninvasive ventilation,[27] which several studies have found very effective for treating even severe levels of hypoxaemia.[28–31] Recently, Kor *et al.*[4] found a 2.6% incidence of ALI in patients undergoing high-risk surgery using a similar definition of impaired oxygen exchange (PaO_2/FIO_2 <40 kPa), but their definition also required the presence of pulmonary infiltrates. It is likely that the higher PRF incidence in our study was due to the fact that the measurable criterion was arterial oxygenation (SpO_2). The incidence of severe PRF in our study (PaO_2/FIO_2 <26.7 kPa regardless of PEEP level) was 0.5%, similar to that seen in previous studies.[6] However, because of the multicentre nature of our study, we cannot rule out that local clinical practices might have led to differences in the distribution of PRF severity. Practices might even have contributed to preventing the development of PRF, or variations in resources might have led to higher rates of rescue failure[32] in some centres. We think it is important for the clinician to note that all levels of postoperative hypoxaemia had an impact on mortality in this cohort (Fig. 2), a finding that confirms that PRF prediction is of great importance.

Four of the seven predictors of PRF risk we identified were related to the patient's health status and these factors accounted for 57% of the total risk. To our knowledge, this is the first study reporting that low preoperative SpO_2 breathing air and even a single respiratory symptom are strongly associated with risk for PRF, although slight oxygen desaturation (SpO_2 ≤95%) has been found to be an independent predictor of a PPC composite outcome.[2]

Table 2 Bivariate analysis of independent predictors in patients with and without postoperative respiratory failure

	Number of patients			Patients without PRF		Patients with PRF		
	Total	%		*n*	%	*n*	%	
Total	5384	100	Missing	5160	95.8	224	4.2	*P*[a]
Variables entered into the multiple regression model								
Sex			0					0.009
Female	2651	49.2		2560	96.6	91	3.4	
Male	2733	50.8		2600	95.1	133	4.9	
Age (years)			0					<0.001
≤ 50	1893	35.2		1853	97.9	40	2.1	
50 to 70	2173	40.4		2072	95.4	101	4.6	
>70	1318	24.4		1235	93.7	83	6.3	
Functional status			0					<0.001
Independent	4823	89.6		4652	96.5	171	3.5	
Partially/totally dependent	561	10.4		508	90.6	53	9.4	
Preoperative length of stay (days)			0					<0.001
<2	4179	77.6		4035	96.6	144	3.4	
≥2	1205	22.4		1125	93.4	80	6.6	
SpO_2 (%)			128					<0.001
≥96	4267	79.3		4143	97.1	124	2.9	
91 to 95	923	17.1		836	90.9	84	9.1	
≤90	66	1.2		54	81.8	12	18.2	
Preoperative respiratory symptoms (at least 1)		0					<0.001	
No	4003	74.3		3909	97.7	94	2.3	
Yes	1381	25.7		1251	90.6	130	9.4	
Smoking exposure (pack-years)			88					0.005
0	2833	52.6		2738	96.6	95	3.4	
1 to 40	2120	39.4		2013	95	107	5	
>40	343	6.4		324	94.5	19	5.5	
Congestive cardiac failure			0					<0.001
No	4543	84.4		4414	97.2	129	2.8	
NYHA I	330	6.1		310	93.9	20	6.1	
NYHA II, III or IV	511	9.5		436	85.3	75	14.7	
Chronic kidney disease[b]			0					<0.001
No	5118	95.1		4919	96.1	199	3.9	
Yes	266	4.9		241	90.6	25	9.4	
Anaemia[c]		167					<0.001	
No	4065	75.5		3920	96.4	145	3.6	
Yes	1152	21.4		1074	93.2	78	6.8	
Liver disease			0					<0.001
No	5075	94.3		4880	96.2	195	3.8	
Yes	309	5.7		280	90.6	29	9.4	
Type of surgery			0					<0.001
Scheduled	4775	88.7		4605	96.4	170	3.6	
Emergency	609	11.3		555	91.1	54	8.9	
Duration of surgery (h)			0					<0.001
<2	3876	72		3768	97.2	108	2.8	
2 to 3	791	14.7		748	94.6	43	5.4	
>3	717	13.3		644	89.8	73	10.2	
Surgical incision			0					<0.001
Peripheral and other	3917	72.8		3811	97.3	106	2.7	
Closed intrathoracic/upper abdominal	685	12.7		658	96.1	27	3.9	
Upper abdominal open	528	9.8		485	91.9	43	8.1	
Intrathoracic open	254	4.7		206	81.1	48	18.9	
Significant variables not entered into the model ($P > 0.05$ or high collinearity, i.e. correlation coefficient >0.25)								
ASA physical status			0					<0.001
1	1204	22.4		1194	99.2	10	0.8	
2	2738	50.8		2673	97.6	65	2.4	
3	1336	24.8		1205	90.2	131	9.8	
4	106	2		88	83	18	17	
BMI ($kg\,m^{-2}$)			0					0.496
<35	5057	93.9		4847	95.8	210	4.2	
≥35	327	6.1		313	95.7	14	4.3	
Smoking status			0					0.007
Never smoker	2833	52.6		2738	96.6	95	3.4	
Current smoker	1242	23.1		1180	95	62	5	
Former smoker	1309	24.3		1242	94.9	67	5.1	
COPD			0					<0.001
No	4864	90		4681	96.6	165	3.4	
Yes	538	10		479	89	59	11	

Table 2 (*continued*)

	Number of patients			Patients without PRF		Patients with PRF		
	Total	%		*n*	%	*n*	%	
Total	5384	100	Missing	5160	95.8	224	4.2	P^a
Cough test[d]			408					<0.001
Negative	3941	73.2		3822	97	119	3	
Positive	1035	19.2		962	92.9	73	7.1	
Respiratory infection in last month			2					0.176
No	5084	94.5		4876	94.6	208	4.1	
Yes	298	5.5		282	95.9	16	5.4	
History of coronary artery disease			0					<0.001
No	4707	87.4		4562	96.9	145	3.1	
Yes	677	12.6		598	88.3	79	11.7	
History of cerebrovascular disease			0					0.001
No	4706	87.4		4525	96.2	181	3.8	
Yes	678	12.6		635	93.7	43	6.3	
Hypertension			0					<0.001
No	3096	57.5		3023	97.6	73	2.4	
Yes	2288	42.5		2137	93.4	151	6.6	
Anaesthetic technique			0					0.025
Neuraxial/Regional	1259	23.4		1219	96.8	40	3.2	
General and combined[e]	4125	76.6		3941	95.5	184	4.5	
Fluid therapy (ml kg^{-1} h^{-1})			0					0.759
≤6	764	14.2		736	96.3	28	3.7	
6 to 9	1017	18.9		977	96.1	40	3.9	
9 to 13	1275	23.7		1223	95.9	52	4.1	
≥13	2328	43.2		2224	95.5	104	4.5	
Intraoperative colloids			0					<0.001
No	4075	75.7		3986	97.8	89	2.2	
Yes	1309	24.3		1174	89.7	135	10.3	
Intraoperative RBC transfusion			0					<0.001
No	5076	94.3		4905	96.6	171	3.4	
Yes	308	5.7		255	82.8	53	17.2	

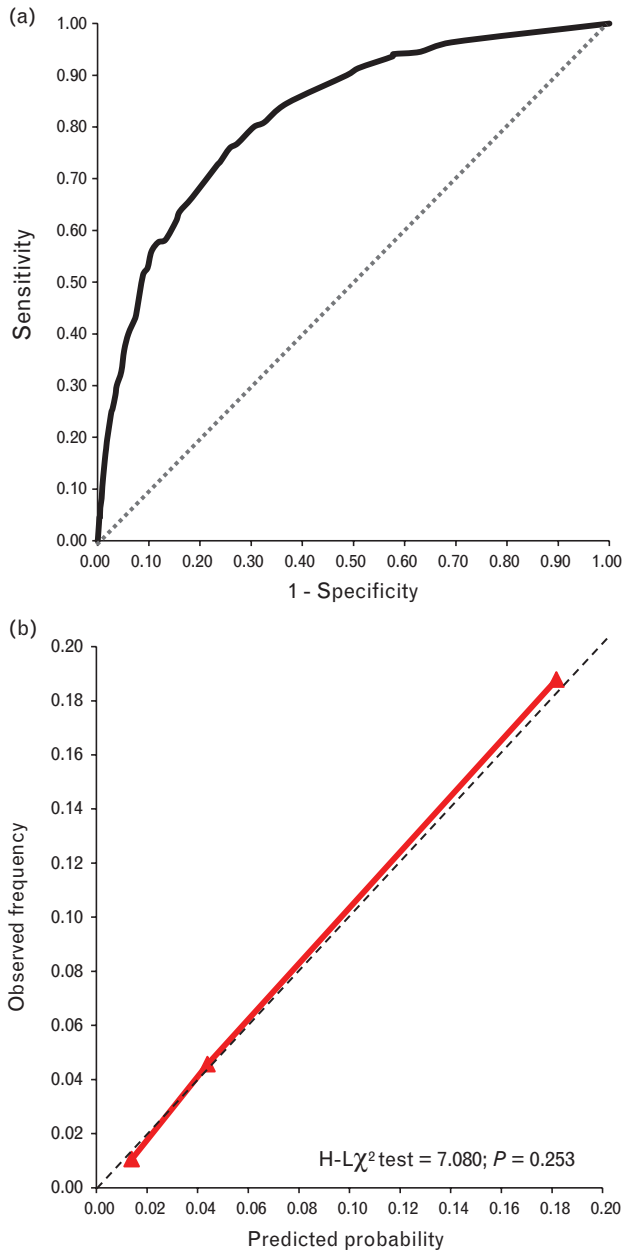
ASA, American Society of Anesthesiologists physical status classification; COPD, chronic obstructive pulmonary disease; NYHA, New York Heart Association classification for chronic heart failure; PRF, postoperative respiratory failure; RBC, red blood cells; SpO_2, peripheral arterial oxygen saturation breathing room air in supine position measured by pulse oximetry. [a] Chi-square test or the Fisher exact test, as appropriate. [b] Renal failure [defined as serum creatinine >2.0 mg dl^{-1} (177 μmol l^{-1})]. [c] In women, <12 g dl^{-1}; in men, <13 g dl^{-1}. [d] In the cough test, the patient is asked to take a deep breath and cough once. A positive test is defined by repeated coughing after the first cough. [e] This category included general anaesthesia alone and general anaesthesia combined with regional blockade.

Table 3 Independent predictors of risk for postoperative respiratory failure as identified by logistic regression[a]

	Bivariate analysis OR (95% CI) ($n = 5384$)	Multivariate analysis OR (95% CI) ($n = 5256$)	β Coefficients	Corrected β coefficients (95% CI)[b]	Risk score[c]
Patient health related factors					
Preoperative SpO_2 (%)					
≥96	1	1			
91 to 95	3.4 (2.5 to 4.5)	2.0 (1.5 to 2.8)	0.704	0.696 (0.380 to 1.007)	7
≤90	7.4 (3.9 to 14.2)	2.7 (1.3 to 2.9)	0.982	0.982 (0.204 to 1.691)	10
Respiratory symptoms (at least 1)	4.3 (3.3 to 5.7)	2.7 (1.9 to 3.6)	0.984	0.983 (0.676 to 1.291)	10
History of congestive heart failure					
No	1	1			
NYHA I	2.2 (1.4 to 3.6)	1.3 (0.8 to 2.2)	0.270	0.273 (−0.281 to 0.775)	3
NYHA ≥II	5.9 (4.4 to 7.9)	2.2 (1.6 to 3.2)	0.806	0.802 (0.442 to 1.154)	8
History of chronic liver disease	2.6 (1.7 to 3.9)	2.1 (1.3 to 3.2)	0.729	0.730 (0.270 to 1.160)	7
Procedure related factors					
Emergency procedure	2.6 (1.9 to 3.6)	3.1 (2.2 to 4.5)	1.144	1.150 (0.777 to 1.511)	12
Surgical incision					
Peripheral	1	1			
Closed intrathoracic/closed upper abdominal	1.5 (1.0 to 2.3)	1.3 (0.9 to 2.1)	0.291	0.303 (−0.171 to 0.743)	3
Open upper abdominal	3.2 (2.2 to 4.6)	1.9 (1.3 to 2.9)	0.667	0.662 (0.247 to 1.062)	7
Intrathoracic open	8.4 (5.8 to 12.1)	3.3 (2.1 to 5.3)	1.195	1.187 (0.715 to 1.649)	12
Duration of surgery (h)					
≤ 2	1	1			
>2 to 3	2.0 (1.4 to 2.9)	1.6 (1.1 to 2.4)	0.453	0.456 (0.046 to 0.849)	5
>3	3.9 (2.9 to 5.4)	2.7 (1.8 to 3.9)	0.983	0.991 (0.601 to 1.372)	10

Due to missing data for some variables, 128 patients were excluded. CI, confidence interval; NYHA, New York Heart Association classification for chronic heart failure; OR, odds ratio; SpO_2, oxyhaemoglobin saturation by pulse oximetry breathing air in supine position. [a] Logistic regression model (*c*-statistic = 0.82; Hosmer–Lemeshow chi-square test = 7.080; $P = 0.253$). [b] After bootstrap resampling (1000 bootstrap subsamples). [c] The simplified risk score was the sum of each corrected β coefficient multiplied by 10 and then rounded.

Fig. 3



The postoperative respiratory failure risk model's performance. Receiver operating characteristics curve (to show discrimination) (a). Agreement between observed frequency and predicted probability at three levels of risk (to assess calibration) (b). Triangles represent the values for risk groups (patients whose scores reflected low, intermediate or high-risk). AUC, area under curve (*c*-statistic); H-L χ^2, Hosmer–Lemeshow chi-square goodness-of-fit test.

Table 4 Sensitivity, specificity and positive and negative likelihood ratios for the ability of the simplified risk score to predict intermediate-risk (≥12 points) and high-risk (≥23 points) cases

	Cut-off ≥12 (95% CI)	Cut-off ≥23 (95% CI)
Sensitivity	84.6% (79.1 to 89.1)	55.9% (49.1 to 62.6)
Specificity	63.3% (61.9 to 64.6)	89.4% (88.6 to 90.3)
Positive likelihood ratio	2.3 (2.2 to 2.5)	5.3 (4.6 to 6.1)
Negative likelihood ratio	0.2 (0.18 to 0.33)	0.5 (0.4 to 0.6)
Positive predictive value	9.1 (7.9 to 10.5)	18.8 (15.9 to 21.9)
Negative predictive value	98.9 (98.5 to 99.3)	97.9 (97.4 to 98.3)

CI, confidence interval.

In addition, clinical prediction using this objective variable is even more precise when three levels of SpO_2 (>95, ≤95 and ≤90%) are considered.[2] In other clinical settings, a low SpO_2 is emerging as a good predictor of outcome.[33,34] The incidence of SpO_2 of 95% or less in our surgical cohort (18.8%) was much higher than the incidence of 6.3% in a recent population-based study.[35] We interpret this as a sign that the surgical population will tend towards impaired cardiorespiratory function. Exclusion of SpO_2 from the score when this measurement is not available (e.g. in clinical settings wherein telephone screening is used) reduces its performance. Calibration suffers in particular, meaning that the model without SpO_2 might not accurately assess level of risk (Supplementary data, Table 2, http://links.lww.com/EJA/A65). We think that routine measurement of preoperative SpO_2 should be encouraged and that it will probably prove to be a robust predictor of poor postoperative outcome.

Preoperative heart failure is a well recognised risk factor for the development of PPCs.[1,5,22] In our study, we analysed three levels of heart failure according to the New York Heart Association (NYHA) classification and found that PRF risk increased with increasing severity of cardiac failure. We also identified chronic liver disease as a predictor of PRF. Chronic liver disease has been linked to a poor postoperative prognosis.[36] One retrospective study found an association between liver disease and unanticipated early postoperative tracheal intubation after nonemergency, noncardiac surgery[5] and a retrospective study identified an 8% rate of ventilatory dependence (postoperative mechanical ventilation >24 h or unplanned intubation) and a similar rate for pneumonia in 733 cirrhotic patients undergoing any surgical procedure.[37] However, chronic liver disease encompasses a wide spectrum of disorders ranging from fatty liver disease to cirrhosis. No study has sought to define a relationship between the different kinds of liver disease and PRF or other PPCs to date. We did not record different types of liver disease in our study, but the strong association we found between this factor and PRF suggests that more detailed records should be used in future studies.

The three remaining independent risk factors were associated with the surgical procedure. In most previous studies, surgical incision, duration of surgery and emergency status have been proposed as predictors of PPCs.[22] However, in the PRF score we present, we further distinguished between open and closed surgery because closed surgery has been associated with less postoperative pneumonia, PRF and mortality.[38] This is consistent with our finding that closed abdominal surgery

approximately halved the risk for PRF and closed thoracic surgery reduced risk fourfold.

Thus, although the identified risk factors differ slightly from study to study, we do see commonalities. Patient-associated risk factors (which depend fundamentally on comorbidity) and procedure-associated risk factors are very similar across the studies. High risk and emergency surgery were identified as risk factors in most of the studies.[1,3,4,7]

A strength of our study is that all variables were chosen and defined *a priori* and cases were identified prospectively by daily searches of records. Moreover, we included patients undergoing a broad spectrum of surgeries rather than limiting the study to a specific patient population or procedure.[39] This approach sought to enhance the reliability of the findings so that they would be generalisable to the real world of anaesthetics and surgery.

A limitation of this study is that postoperative follow-up ended at hospital discharge. Second, the cohort was recruited by volunteer hospitals that did not cover the entire territory of Europe. Third, possible intraoperative events that might be related to PRF, such as respiratory complications, blood loss or ventilatory management, were not taken into account. Fourth, the present study reports internal validation of the score; external validation remains to be performed.

Identifying patients at a high risk for developing PRF is of great value in clinical decision making about perioperative measures to be applied. Among the measures that have been shown to reduce the incidence of PRF, we mention preoperative optimisation of some health conditions such as smoking and alcohol cessation,[40,41] intraoperative ventilatory management[42–44] and postoperative analgesia and physiotherapy.[45,46] Although strategies to reduce PRF risk have also been shown to reduce health costs,[47–50] randomised trials to test the efficacy of preventive measures are still lacking. The PERISCOPE-PRF score developed in this study can be useful for classifying patients systematically in such trials.

In conclusion, PRF is a frequent complication and is associated with a poor prognosis, but the PERISCOPE-PRF score is likely to help identify surgical patients at risk so that stricter measures to prevent this life-threatening complication can be considered.

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Appendix

List of Participating Centres and Contributors to the PERISCOPE Cohort Study

Chief Investigator

Jaume Canet, Hospital Universitari Germans Trias i Pujol, Barcelona, Spain

Steering Committee Members

Jaume Canet, Spain

Sergi Sabaté, Spain

Olivier Langeron, France

Marcelo Gama de Abreu, Germany

Lluís Gallart, Spain

F. Javier Belda, Spain

Paolo Pelosi, Italy

Andreas Hoeft, Germany

Valentin Mazo, Spain

Off-site Data Management

Brigitte Leva, European Society of Anaesthesiology aisbl (Brussels), Belgium

Albania

University Hospital centre ''Mother Theresa'' (Tirana): Jonela Burimi, Toma Halefi, Aleksander Hoxha*, Kliti Pilika, Imelda Selmani

Belgium

Cliniques Universitaires Saint Luc A.S.B.L Université Catholique de Louvain (Brussels): Véronique Daout, Caroline Gauthier, David Kahn, Mona Momeni*, Christine Watremez

Bosnia and Herzegovina

Clinical Centre University Sarajevo ''Heart Centre'' (Sarajevo): Slavenka Straus*

General Hospital ''Prim.dr Abdulah Nakas''(Sarajevo): Dejana Djonovic-manovic, Marina Juros-Zovko*

Croatia

University Hospital Rijeka (Rijka): Helga Komen-Ušljebrka*, Vlasta Orlić, Ivana Stuck

Czech Republic

Faculty Hospital Brno (Brno): Lenka Baláková, Martina Kosinová, Ivo Křikava, Roman Štoudek, Petr Štourač*, Katarina Zadražilová

Masaryks hospital Usti nad labem (Usti Nad Labem): Sanober Janvekar*

Estonia

Tartu University Hospital (Tartu): Juri Karjagin, Kadri Rõivassepp, Alar Sõrmus*

France

Hôpital Pitié-Salpêtrière (Paris): Philippe Cuvillon, Cristina Ibáñez-Esteve, Olivier Langeron*, Mathieu Raux, Armelle Nicolas-Robin

Germany

Klinikum Darmstadt GmbH (Darmstadt): André Winter*

Medical Centre of the Johannes Gutenberg University Mainz (Mainz): Malte Brunier, Kristin Engelhard, Rita Laufenberg Feldmann*, Raphaele Lindemann, Susanne Mauff, Anne Sebastiani, Camila Zamperoni

University Hospital Bonn (Bonn): Andreas Hoeft*, Florian Kessler, Maria Wittmann

University Hospital Carl Gustav Carus - Dresden University of Technonology (Dresden): Thomas Bluth, Marcelo Gama de Abreu*, Andreas Güldner, Thomas Kiss

Hungary

MISEK Kft. (Miskolc): Kristina Bráz, Csilla Ruszkai*

Italy

Azienda Ospedaliera (Padova): Massimo Micaglio, Carlo Ori, Matteo Parotto*, Paolo Persona

Azienda Ospedaliera S. Croce e Carle (Cuneo): Coletta Giuseppe*

Azienda USL n. 5 di Pisa Ospedale F. Lotti (Pontedera): Paolo Carnesecchi, Denise Lazzeroni, Irene Lorenzi*

European Institute of Oncology (Milano): Gianluca Castellani, Daniele Sances*, Gianluca Spano, Stefano Tredici, Dario Vezzoli

IRCCS San Martino (Genova): Iole Brunetti, Anna Di Noto, Angelo Gratarola, Alexandre Molin*, Luca Montagnani, Giulia Pellerano, Paolo Pelosi

Ospedale Sant'Orsola - Malpighi (Bologna): Maurizio Fusari*

University of Insubria (Varese): Laura Camici, Luca Guzzetti, Fabio Marangoni, Paolo Severgnini*

University of Milano, Ospedale San Paolo (Milano): Piero Di Mauro, Francesca Rapido, Concezione Tommasino*

Latvia

Pauls Stradins Clinical University hospital (Riga): Ieva Nemme, Janis Nemme*

Lithuania

Kaunas Medical University Hospital (Kaunas):, Justinas Blieka, Jurgita Borodičienė, Brigita Budrytė, Aurika Karbonskiene*, Inga Kiudulaitė, Eglė Milieškaitė, Renata Rasimavičiūtė, Ugnė Sirevičienė, Ramunė Stašaitytė, Edgaras Usas, Giedrė Zarskienė

Vilnius University Hospital Santariskiu Clinics (Vilnius): Egle Kontrimaviciute, Jurate Sipylaite*, Gabija Tomkutė

Luxembourg

ZithaKlinik(Luxembourg): Petra Bardea, Marco Klop, Marc Koch*

Poland

10 Wojskowy Szpital Kliniczny z Polikliniką w Bydgoszczy (Bydgoszcz): Dominika Bożiłow, Robert Goch*

Portugal

Hospitais da Universidade de Coimbra, EPE. (Coimbra): João Bonifácio, Sofia Marques, Tânia Teresa dos Santos Ralha*

Centro Hospitalar de Lisboa Ocidental (Lisbon): Daniel Alves, Inês Carvalho, Josefina Suzana Da Cruz Parente*, Sara Tomé

Hospital Fernando Fonseca (Lisbon): Cristina Carmona*

Instituto Português de Oncologia Do Porto (Porto): Miranda Costa*, Maria Lina, Sofia Sierra

Romania

Emergency Clinical Hospital of Constanta (Constanta): Alina Balcan, Iulia Cindea, Viorel Ionel Gherghina*, Catalin Grasa

Emergency County Hospital Clinic of Anaesthesia and Intensive Care (Târgu Mures): Ruxandra Copotoiu, Sanda-Maria Copotoiu*, Judit Kovacs*, Janos Szederjesi, Arthur Theil

Emergency Institute of Cardiovascular Diseases Prof Dr C. C. Iliescu (Bucharest): Daniela Filipescu*

Russia

Krasnoyarsk State Medical University (Krasnoyarsk): Alexey Grytsan*, Tatiana Kapkan, Sergey Rostovtsev, Anastasia Yushkova

Spain

Clinica Universidad de Navarra (Pamplona): Ricardo Calderón, Elena Cacho, Carolina Marginet, Pablo Monedero*, Maria José Yepes

Consorcio Hospital General Universitario de Valencia (Valencia): Jose Miguel Esparza Miñana, Manuel Granell Gil*, Gabriel Rico Portolés

Corporació Sanitària Parc Taulí (Barcelona Sabadell): Alberto Lisi*, Gisela Perez, Nuria Poch

Fundacio Althaia (Manresa): Mauricio Roberto Argañaraz Quinteros, Carme Font Bosch, Jordi Torrellardona Llobera*

Fundació Puigvert (Barcelona): Sergi Sabaté*, Pilar Sierra

Hospital Arnau de Vilanova (Lleida): Mercedes Matute*

Hospital Clinic de Barcelona (Barcelona): Amalia Alcon Dominguez*, María José Arguis, Isabel Belda, Enrique Carrero, Jacobo Moreno, Irene Rovira, Marta Ubre, Roberto Castillo, Sílvia Herrero

Hospital Clínic Universitari de Valencia (Valencia): Maria Teresa Ballester Luján*, F.Javier Belda, José Carbonell, Geri Gencheva, Andrea Gutierrez, Julio Llorens, Sofia Machado

Hospital de Denia (Denia): Francisca Llobell*, Daniel Paz Martin

Hospital del Tajo Aranjuez (Madrid): Francisco Javier García-Miguel*

Hospital General de La Palma Breña Alta (La Palma, Canarias): Aníbal Pérez García*

Hospital General Universitario Alicante (Alicante): Roque Company*, Aixa Ahamdanech Idrissi, Josefina del Fresno Cañaveras, Jose Alejandro Navarro Martinez; Estefania Paya Martinez, Ester Sanchez Garcia

Hospital San Jorge (Huesca); Jorge Vera Bella*

Hospital Sant Pau (Barcelona): Inmaculada India Aldana, J. Manuel Campos, Xavier Pelaez Vaamonde*

Hospital Santa Maria (Lleida): Montserrat Torra*

Hospital Universitari del Mar 'Parc de Salut Mar (Barcelona): Raquel Arroyo, Juan Carlos Cabrera, Jesús Carazo Cordobes*, Lluís Gallart, Amelia Rojo, Francisco Javier Santiveri

Hospital Universitari Germans Trias i Pujol (Badalona): Jaume Canet*, Miriam González, Anabel Jiménez, Yolanda Jiménez, Agnès Martí, Valentin Mazo, Enrique Moret, Monica Rodriguez Nuñez*, Joaquin Velasco

Hospital Universitario 12 de Octubre (Madrid): Adriana Calderón, Matide González, Olga González, Ana Hermira Anchuelo*, Eloisa López, Esther Sánchez

Hospital Universitario de La Princesa (Móstoles-Madrid): Blanca Aznárez Zango*, Francisco José García Corral, Esperanza Mata Mena, Antonio Planas Roca

Hospital Universitario de Móstoles (Madrid): Raquel Fernández Rocío Ayala Soto*, Borja Quintana

Hospital Universitario Marques De Valdecilla (Santander): Jose Manuel Rabanal Llevot*, Mónica Mercedes Williams Camus, Alba Palacios Blanco, Angela Largo Ruiz

Hospital Universitario Rio Hortgea (Valladolid): Jesus Rico Feijoo*

Hospital Universitario Virgen del Rocio (Sevilla): Elvira Castellano Garijo*

Hospital Son Llatzer (Palma de Mallorca): Julio Belmonte Cuenca*, Marcos José Bonet Binimelis, Ivaylo Grigorov, Josep Lluis Aguilar

Vall d'Hebron University Hospital (Barcelona): Míriam De Nadal Clanchet, Encarnación Guerrero Viñas, Susana Manrique Muñiz, Víctor Martín Mora, Francisca Munar Bauzà, Sonia Núñez Aguado, Montserrat Olivé Vidal*, María luisa Paños Gozalo, Marcos Sánchez Marín, María Carmen Suescun López

Switzerland

Ospedale Regionale di Lugano (Lugano): Paolo Maino*

Ukraine

St.Katherine Hospital of Cardiology (Odessa): Yevhen Eugene Yevstratov*

Turkey

Medical Faculty of Istanbul, Istanbul University (Istanbul): Semra Kucukgoncu, Nuzhet Mert Sentürk*, Zerrin Sungur Ulke

*Site leader.