

Marc Leone
Carole Bechis
Karine Baumstarck
Alexandre Ouattara
Olivier Collange
Pascal Augustin
Djillali Annane
Charlotte Arbelot
Karim Asehnoune
Olivier Baldési
Simon Bourcier
Laurence Delapierre
Didier Demory
Baptiste Hengy
Carole Ichai
Eric Kipnis
Etienne Brasdefer
Sigismond Lasocki
Matthieu Legrand
Olivier Mimoz
Thomas Rimmelé
Jugurtha Aliane
Pierre-Marie Bertrand
Nicolas Bruder
Fanny Klasen
Emilie Friou
Bruno Lévy
Oriane Martinez
Eric Peytel
Alexandra Piton
Elisa Richter
Kamel Toufik
Marie-Charlotte Vogler
Florent Wallet
Mourad Boufi
Bernard Allaouchiche
Jean-Michel Constantin
Claude Martin
Samir Jaber
Jean-Yves Lefrant

Outcome of acute mesenteric ischemia in the intensive care unit: a retrospective, multicenter study of 780 cases

Received: 19 December 2014
Accepted: 5 February 2015

© Springer-Verlag Berlin Heidelberg and
ESICM 2015

Take-home message: Acute mesenteric ischemia was associated with a 58 % death rate in ICU patients. Age and severity score at diagnosis were risk factors for mortality; plasma lactate concentration above 2.7 mmol/l was also an independent risk factor.

For the AtlanRea and AzuRea Collaborative Network Investigators; members are listed in the “Appendix”.

Electronic supplementary material

The online version of this article (doi:10.1007/s00134-015-3690-8) contains supplementary material, which is available to authorized users.

A. Piton
Anesthesiology and Critical Care
Department, University Hospital of
Toulouse, University Toulouse 3 Paul
Sabatier, Toulouse, France
e-mail: alexandra.piton@hotmail.fr

E. Peytel
Service de Reanimation, Hôpital
d’Instruction des Armées Laveran,
Marseille, France
e-mail: eric.peytel@wanadoo.fr

K. Toufik
Medical-surgical Intensive Care Unit,
Hôpital de La Source, Centre Hospitalier
Régional d'Orléans, Orléans, France
e-mail: toufik.kamel@chr-orleans.fr

M.-C. Vogler
Service d'anesthésie réanimation,
hôpital Nord, CHU de Saint Etienne,
Saint-priest-en-Jarez, France
e-mail: vogler.mariecharlotte@hotmail.fr

F. Wallet · B. Allaouchiche
Department of Anesthesia and Critical Care
Medicine, Lyon-Sud Hospital, Hospices
Civils de Lyon and University Lyon 1,
Lyon, France
e-mail: florent.wallet@gmail.com

B. Allaouchiche
e-mail: bernard.allaouchiche@chu-lyon.fr

M. Leone (✉) · C. Bechis · C. Martin
Service d'anesthésie et de réanimation,
hôpital Nord, Assistance Publique Hôpitaux
de Marseille, Aix Marseille Université,
Chemin des Bourrely, 13015 Marseille,
France
e-mail: marc.leone@ap-hm.fr
Tel.: +33491968650

K. Baumstarck
Unité d'Aide Méthodologique à la
Recherche Clinique et Epidémiologique,
Aix Marseille Université, Marseille, France

A. Ouattara
CHU de Bordeaux, Service d'Anesthésie-
Réanimation II, Unité de Réanimation
polyvalente de la Maison du Haut-Lévêque,
Hôpital Haut Lévêque, Avenue Magellan,
33600 Pessac, France
e-mail: alexandre.ouattara@chu-
bordeaux.fr

O. Collange
Pôle Anesthésie, Réanimation Chirurgicale,
SAMU, Hôpitaux Universitaires de
Strasbourg, Strasbourg, France
e-mail: olivier.collange@chru-strasbourg.fr

P. Augustin
Département d'Anesthésie Réanimation
Chirurgicale, CHU Bichat Claude Bernard,
46 Rue Henri Huchard, Paris, France
e-mail: pascalaugustin@hotmail.com

D. Annane
Department of Intensive Care Medicine,
Raymond Poincaré Hospital, Assistance
Publique-Hôpitaux de Paris, Garches,
France
e-mail: djillali.annane@rpc.aphp.fr

D. Annane
University of Versailles, Montigny le
Bretonneux, France

C. Arbelot
Réanimation Chirurgicale Polyvalente,
Département d'Anesthésie et de
Réanimation, Hôpital Pitié Salpêtrière
APHP, Paris, France
e-mail: charlotte.arbelot@psl.aphp.fr

K. Asehnoune
Department of Anesthesiology and Critical
Care, Hôtel Dieu, 1 place Alexis Ricordeau,
Nantes Cedex 1, France
e-mail: karim.asehnoune@chu-nantes.fr

O. Baldesi
Service de réanimation, Centre Hospitalier
d'Aix-en-Provence, Aix-en-Provence,
France
e-mail: obaldesi@ch-aix.fr

P.-M. Bertrand
Service de Réanimation, Centre Hospitalier
de Cannes, Cannes, France

S. Bourcier
Medical Intensive Care Unit, Cochin
Hospital, Groupe Hospitalier Cochin Broca
Hôtel-Dieu, Assistance Publique des
Hôpitaux de Paris, 27 rue du Faubourg,
Saint-Jacques, Paris, France
e-mail: simon_bourcier@hotmail.com

N. Bruder
Département d'Anesthésie et de
Réanimation, Hôpital la Timone,
Assistance Publique Hôpitaux de Marseille,
Aix Marseille Université, Marseille,
France

L. Delapierre
Service de Réanimation Polyvalente, CH
Henri Duffaut, 305, rue Raoul Follereau,
Avignon Cedex09, France
e-mail: ldelapierre@ch-avignon.fr

D. Demory
Service Réanimation Polyvalente-USC,
Hôpital Sainte Musse, Avenue Sainte Claire
Deville, Toulon, France
e-mail: didier.demory@ch-toulon.fr

E. Friou
Department of Medical Intensive Care and
Hyperbaric Medicine, University Hospital
of Angers, 4 rue Larrey, Angers, France
e-mail: emilie.friou@yahoo.fr

B. Hengy · T. Rimmelé
Département d'anesthésie-réanimation,
Hôpital Edouard Herriot, Place d'Arsonval,
Lyon, France
e-mail: baptiste.hengy@chu-lyon.fr

T. Rimmelé
e-mail: thomas.rimmele@chu-lyon.fr

C. Ichai
Réanimation médico-chirurgicale, Hôpital
Saint-Roch, CHU de Nice, Nice, France
e-mail: ichai@unice.fr

E. Kipnis · E. Brasdefer
Surgical Critical Care Unit, Department of
Anesthesiology and Critical Care, Lille
University Teaching Hospital-CHU Lille,
Lille, France
e-mail: ekipnis@gmail.com

E. Brasdefer
e-mail: etienne.brasdefer@chru-lille.fr

F. Klasen
Medical Intensive Care Unit, CHU Nord,
Assistance Publique Hôpitaux de Marseille,
Aix Marseille University, Marseille, France
e-mail: fanny.klasen@ap-hm.fr

S. Lasocki
Pôle d'anesthésie-réanimation, CHU
d'Angers, 4, rue Larrey, Angers, France
e-mail: sigismond@lasocki.com

J. Aliane
Service de Réanimation Médicale, Hôpital
Gabriel Montpied, CHU de Clermont-
Ferrand, Clermont-Ferrand, France

M. Legrand
Department of Anesthesiology and Critical
Care and SMUR and Burn Unit, Assistance
Publique-Hôpitaux de Paris, GH St Louis
Lariboisière, University of Paris 7 Denis
Diderot, Paris, France

O. Mimoz
Service d'Anesthésie Réanimation, CHU de
Poitiers, INSERM U1070, Université de
Poitiers, Poitiers, France
e-mail: o.mimoz@chu-poitiers.fr

B. Lévy
Service de Réanimation Médicale Brabois,
Hôpital Brabois, CHU Nancy, Vandoeuvre-
Les-Nancy, France
e-mail: blevy5643@gmail.com

O. Martinez
Department of Anesthesiology and Critical
Care Medicine, Lapeyronie University
Hospital, Montpellier University 1,
Montpellier, France

E. Richter
Département d'Anesthésie et de
Réanimation, Hôpital la Conception,
Assistance Publique Hôpitaux de Marseille,
Aix Marseille Université, Marseille, France
e-mail: elisa.richter@ap-hm.fr

M. Boufi
Service de chirurgie vasculaire, hôpital
Nord, Assistance Publique Hôpitaux de
Marseille, Aix Marseille Université,
Marseille, France
e-mail: mourad.boufi@ap-hm.fr

J.-M. Constantin
Réanimation Adultes et Unité de Soins
Continus, CHU Estaing, CHU Clermont-
Ferrand, 1 Place Lucie-et-Raymond-
Aubrac, Clermont-Ferrand, France
e-mail: jmconstantin@chu-
clermontferrand.fr

S. Jaber
Intensive Care Unit, Anaesthesia and
Critical Care Dept B, Saint-Elloi Teaching
Hospital, INSERM U1046, Montpellier
1 University, Montpellier, France
e-mail: s-jaber@chu-montpellier.fr

J.-Y. Lefrant
Services des Réanimations, Division
Anesthésie Réanimation Douleur Urgence,
CHU de Nîmes, place du Pr-Robert-Debré,
Nîmes, France
e-mail: jean-yves.lefrant@wanadoo.fr

Abstract Background: In the intensive care unit (ICU), the outcomes of patients with acute mesenteric ischemia (AMI) are poorly documented. This study aimed to determine the risk factors for death in ICU patients with AMI. **Methods:** A retrospective, observational, non-interventional, multicenter study was conducted in 43 ICUs of 38 public institutions in France. From January 2008 to December 2013, all adult patients with a diagnosis of AMI during their hospitalization in ICU were included in a database. The diagnosis was confirmed by at least one of three procedures (computed tomography scan, gastrointestinal endoscopy, or upon surgery). To determine factors associated with ICU death, we established a logistic regression model. Recursive partitioning analysis was applied to construct a decision tree regarding risk factors and their interactions most critical to determining outcomes. **Results:** The death rate of the 780 included patients was 58%. Being older, having a higher sequential organ failure assessment (SOFA)

severity score at diagnosis, and a plasma lactate concentration over 2.7 mmol/l at diagnosis were independent risk factors of ICU mortality. In contrast, having a prior history of peripheral vascular disease or an initial surgical treatment were independent protective factors against ICU mortality. Using age and SOFA severity score, we established an ICU mortality score at diagnosis based on the cutoffs provided by recursive partitioning analysis. Probability of survival was statistically different ($p < 0.001$) between patients with a score from 0 to 2 and those with a score of 3 and 4. **Conclusion:** Acute mesenteric ischemia in ICU patients was associated with a 58% ICU death rate. Age and SOFA severity score at diagnosis were risk factors for mortality. Plasma lactate concentration over 2.7 mmol/l was also an independent risk factor, but values in the normal range did not exclude the diagnosis of AMI.

Keywords Ischemia · Mesenteric · Occlusion · Lactate · Surgery

Introduction

Acute mesenteric ischemia (AMI) is subdivided into several forms according to the mechanism of inadequate blood flow. Arterial emboli are responsible for approximately 50% of cases. Most arterial emboli are cardiac in origin, resulting in a dramatic onset of symptoms. Arterial thrombosis constitutes 25–30% of all ischemic events. Arterial thrombosis develops in patients with severe atherosclerotic disease. Most patients can tolerate major visceral artery obstruction because of the slow progressive nature of atherosclerosis. Approximately 20% of patients with AMI have nonocclusive mesenteric ischemia, probably related to low cardiac output associated with diffuse mesenteric vasoconstriction [1].

The outcomes of ICU patients with AMI are poorly reported. The sparse data available related to AMI concerns patients undergoing surgery. The operative mortality of patients with AMI ranges from 26 to 72%

[2]. In these surgical patients, the risk factors for death include preoperative do not resuscitate orders, open wounds, low albumin, contaminated versus clean-contaminated cases, and poor functional status [3]. Thus, AMI is associated with high mortality. Early diagnosis and extensive knowledge of risk factors for death are important issues, which by being addressed may contribute to decreased mortality [1–3]. However, previous studies did not clearly identify patients either diagnosed with AMI in the ICU or requiring ICU.

Improving the knowledge about the outcomes of ICU patients with AMI would allow one to provide accurate information to both patients and their relatives, planning appropriate management and designing future clinical trials. We hypothesized that AMI is associated with high mortality in ICU patients. Therefore, the aim of our study was to assess the mortality associated with AMI in ICU patients and the risk factors associated with ICU mortality. Finally, we developed a score aimed at predicting ICU mortality in patients with AMI.

Methods

Study design and population

We conducted a retrospective, observational, non-interventional, multicenter study in 43 ICUs from 38 public healthcare institutions. These 43 institutions belonged to different networks of ICUs. Of note, initially, 46 ICUs were contacted and three units declined to participate. All adult patients with a diagnosis of AMI were screened. Retrospectively from December 2013, each participating ICU included all consecutive patients with a diagnosis of AMI until reaching a maximum of 25 inclusions. The inclusion period ranged from January 2008 to December 2013. Patients were included if at least one of the three diagnostic procedures (computed tomography scan, gastrointestinal endoscopy, or surgery) supported the diagnosis of AMI.

Ethics and consent

As an observational, non-interventional, retrospective study, according to French legislation (articles L.1121-1 paragraph 1 and R1121-2, Public Health Code), neither informed consent nor approval of the ethics committee was required to use data from patient records for an epidemiologic study. All data were collected anonymously from medical records only. Data representing patient identifiers were not collected.

Data collection

Cases of AMI were identified using the French national healthcare system administrative coding for diagnosis (K550). The data were retrospectively collected from patient records, either electronic or paper. At ICU admission, we collected demographics, reasons for admission, simplified acute physiology score (SAPS) II, and presence of peripheral vascular disease or cancer.

From admission to AMI diagnosis, we collected the following data: time between ICU admission and AMI diagnosis, recent vascular surgery, use of vasopressors in the 24 h prior to AMI diagnosis, type of vasoactive drugs, maximal dose of vasoactive drug, any type of shock 10 days prior to AMI diagnosis, anticoagulation (type), atrial fibrillation, duration of mechanical ventilation prior to AMI diagnosis, and route of feeding (enteral or parenteral).

On the day of AMI diagnosis, we collected the diagnostic procedure(s) for AMI (requiring written diagnosis of AMI on the reports of computed tomography (CT) scan, gastrointestinal (GI) endoscopy, or surgery), date of diagnosis, type of ischemia (following aortic surgery/intravascular procedures or spontaneous), administration of antimicrobial treatment, sequential organ failure assessment score (SOFA) [4], and plasma lactate concentration.

For each patient, we also identified four events reflecting organ failure: use of renal replacement therapy (renal failure), need for inotrope or central venous oxygen saturation below 70 % (heart failure), platelet count under 100 G/l (coagulation failure), and prothrombin time ratio under 50 % (liver failure).

From the day of AMI diagnosis to the ICU discharge (or ICU death), we reported the duration of antimicrobial treatment, duration of vasoactive drug support, maximum dosage of vasoactive drug, initial surgical procedure (i.e., in the first 24 h of AMI diagnosis), any additional diagnostic imaging procedures, anticoagulation (type), plasma lactate concentration measured 24 h after the AMI diagnosis, duration of mechanical ventilation following AMI diagnosis, route of feeding (enteral or parenteral), and ICU outcome (survivors or nonsurvivors).

Statistical analysis

Statistical analyses were performed using the SPSS 15.0 software package (SPSS Inc., Chicago, IL). For continuous and ordinal variables, data were expressed as mean with standard deviation or median with interquartile range. Two groups were defined according to ICU outcome, namely survivors or nonsurvivors. The comparison between the two groups was performed on continuous variables using Student *t* tests or Mann–Whitney tests and on qualitative variables using Chi square or Fisher's exact tests.

The discriminative performance of plasma lactate concentration at diagnosis, plasma lactate concentration at 24 h, and the change in plasma lactate concentrations between diagnosis and 24 h were assessed through receiver operating characteristics (ROC) curve analysis. The optimal cutoff values were defined by the value of the Youden index (sensitivity + specificity – 1). Kaplan–Meier survival analyses were performed to estimate the probability of survival following ICU admission. Comparisons of probabilities of survival were performed using log-rank test according to plasma lactate concentration levels (≤ 3 , >3 and ≤ 9 , and >9 mmol/l) and number of organ failures (0–2 vs. 3–4).

To determine factors potentially associated with ICU death, a logistic regression model was established using nine variables: age, prior history of cancer, prior history of peripheral vascular disease, shock in the 10 days prior to AMI diagnosis, SOFA at AMI diagnosis, plasma lactate concentration at AMI diagnosis, antimicrobial administration, initial surgical treatment, and time between ICU admission and AMI diagnosis. The variables relevant to the model were selected by their clinical and/or statistical relevance (previously reported as risk factors and/or $p < 0.05$ from the univariate analysis). The final model expressed the odds ratios (OR) and 95 % confidence intervals (CI).

ICU mortality score

Recursive partitioning analysis (RPA) was applied to determine outcome groups of ICU survival from the major well-known risk factors using the RPART routine in R software (Package 'rpart', Recursive Partitioning and Regression Trees. 2014) [5]. RPA is a method of classification providing homogeneous groups of individuals based on the status of the outcome (ICU nonsurvivor or ICU survivor). This method creates a decision tree according to risk factors and their interactions that are most important in determining outcome [6]. The optimal cutoffs of the variables were provided by the RPA. The initial continuous variables were transformed into categorical variables from these cutoffs; points were arbitrarily allocated to each category to be as intuitive as possible. The total score ranged from 0 to 4 (lower to higher risk of ICU mortality). The discriminative performance of the score was determined from ROC analysis. The optimal cutoff value was defined by the Youden index. Kaplan–Meier survival analysis was performed to estimate the probability of survival following ICU admission, and comparison between individuals under and over the optimal cutoff value was assessed using the log-rank test.

Results

In 43 ICUs, 780 patients were included in the database. ICU death occurred in 454 (58 %) patients. The in-hospital death rate was 63 %. Each ICU included 19 ± 13 patients. Patient characteristics are reported in Table 1. At ICU admission, patients were 71 (61–79) years of age, with a median SAPS II of 59 (46–74). Concerning prior medical history, peripheral arterial disease, vascular surgery, and cancer were reported in 44, 32, and 21 % of patients, respectively. In the 24 h prior to AMI diagnosis, vasopressors were administered to 44 % of patients. Anticoagulants were used in 51 % of patients. Feeding was given via either enteral (49 %) or parenteral (12 %) routes.

The time between ICU admission and AMI diagnosis was 0 (0–1) day in survivors and 1 (0–3) day in nonsurvivors ($p = 0.1$). At the AMI diagnosis, atrial fibrillation was found in 25 % of patients. It was identified in 23 % of patients with “spontaneous” AMI and 33 % of those with AMI occurring after vascular surgery ($p = 0.04$). The median SOFA score was 10 (7–13). The mean plasma lactate concentration was 4.0 ± 3.3 mmol/l in survivors and 6.6 ± 5.1 mmol/l in nonsurvivors ($p < 0.001$). Mean plasma lactate was under 2 mmol/l in 23 % of patients overall and 16 % of nonsurvivors. The best cutoff value of plasma lactate concentration at

diagnosis of AMI to discriminate survivors from nonsurvivors was 2.7 mmol/l (Fig. 1a). At this threshold, plasma lactate had a sensitivity of 77 %, a specificity of 50 %, and a Youden index of 0.27. At 24 h, the best cutoff value was 3.9 mmol/l with a sensitivity of 60 %, a specificity of 83 %, and a Youden index of 0.43. In contrast, the variations of plasma lactate concentrations between diagnosis and 24 h did not differ between survivors and nonsurvivors (Fig. 1b). As shown by Fig. 2a, survival differed between patients according to plasma lactate concentration measured at diagnosis of AMI. Of note, the plasma lactate concentration decreased in patients undergoing surgery and increased in those not undergoing surgery, although the difference did not reach statistical significance ($p = 0.48$).

Concerning diagnostic procedures for AMI, CT scan, surgery, and endoscopy were used in 58, 27, and 15 % of patients, respectively. Antibiotics, vasopressors, and anticoagulants were used in 79, 79, and 72 % of patients, respectively. The duration of antibiotic treatment was 6.5 ± 5.8 days. Following AMI diagnosis, heart failure, liver failure, thrombocytopenia, and renal replacement therapy were reported in 31, 46, 28, and 45 % of patients, respectively (Table 2). Figure 2b shows that the cumulative number of these events impacted survival. Time to death after diagnosis was 11 (9–13) days.

Several variables differed between ICU survivors and nonsurvivors. Using a logistic regression model comprising nine risk factors (age, prior history of cancer, prior history of peripheral vascular disease, shock in the 10 days prior to AMI diagnosis, SOFA at diagnosis, plasma lactate concentration at diagnosis, antimicrobial administration, initial surgical treatment, time from ICU admission to AMI diagnosis), we identified five independent variables associated with increased risk of ICU death (Table 3). Being older, having a higher SOFA score at AMI diagnosis, and plasma lactate concentration over 2.7 mmol/l (optimal cutoff value) at AMI diagnosis were independent risk factors of ICU mortality. In contrast, having a prior history of peripheral vascular disease and an initial surgical treatment were independent protective factors against ICU mortality. In Supplemental Tables 1 and 2 we identified the results of the univariate analysis in the 176 patients who did not undergo initial surgical treatment and the 604 patients undergoing initial surgical treatment.

Using age and SOFA score, we developed an ICU mortality score at diagnosis based on the cutoffs provided by the RPA method (Supplemental Table 3). Plasma lactate concentrations, history of peripheral vascular disease, and initial treatment were excluded from the score because they could not adequately discriminate patient outcome given the low number of patients per group (less than 20). Probability of survival was statistically different ($p < 0.001$) between individuals with a score from 0 to 2 and those with a score of 3 and 4 (Fig. 2c).

Table 1 Features of patients according to their outcomes in intensive care unit

	MD	Total (n = 780)	Survivors (n = 326)	Nonsurvivors (n = 454)	p
Demographics					
Gender					
Male (%)	0	58	58	58	0.961
Age (years)					
Mean ± SD	0	69 ± 14	66 ± 15	71 ± 12	0.001
History					
PVD (%)	2	44	44	43	0.904
Cancer (%)	1	21	15	25	0.001
Vascular surgery (%)	0	32	35	29	0.07
Reasons for ICU admission					
Medical (%)	0	30	18	38	0.001
Planned surgery (%)		13	14	13	
Urgent surgery (%)		54	66	46	
Trauma (%)		3	3	3	
SAPS II					
Median (IQR)	15	59 (46–74)	48 (37–62)	66 (53–80)	0.001
Diagnosis day					
Shock (<10 days) (%)	17	38	32.7	41.9	0.01
Diagnosis					
CT scan (%)	4	58	63	54	0.016
GI endoscopy (%)		15	16	15	
Surgery (%)		27	21	31	
Type of ischemia					
No surgery (%)	0	73	71	74	0.320
Aorta surgery (%)		27	28	26	
Cardiac surgery (%)		0.5	0.9	0.2	
Atrial fibrillation (%)	2	25	26	25	0.873
SOFA					
Median (IQR)	74	10 (7–13)	8 (4–11)	11 (9–14)	0.001
Lactate (mmol/l)					
Mean ± SD	76	5.6 ± 3.6	4.0 ± 3.3	6.6 ± 5.1	0.001
Platelet (G/l)					
Mean ± SD	15	185 ± 130	214 ± 140	165 ± 117	0.001
ICU stay					
Lactate 24 h (mmol/l)					
Mean ± SD	159	5.1 ± 5.1	2.8 ± 2.3	7.1 ± 5.7	0.001
Heart failure (%)					
Inotrope or ScvO ₂ < 70 %	32	31	21	37	0.001
Liver failure (%)					
PT < 50 % or jaundice	10	46	30	58	0.001
Renal failure (%)					
RRT	2	45	33	55	0.001

CT computed tomography, GI gastrointestinal, ICU intensive care unit, IQR interquartile range, MD missing data, p p value between survivors and nonsurvivors, PT prothrombin time, PVD peripheral

vascular disease, RRT renal replacement therapy, SAPS simplified acute physiology score, ScvO₂ central venous oxygen saturation, SD standard deviation, SOFA sequential organ failure assessment

Discussion

From the present database, 58 % of ICU patients with AMI did not survive their ICU stay. Variables, which were associated with death, included age, SOFA score at admission, and plasma lactate concentration above 2.7 mmol/l at diagnosis of AMI. Prior history of peripheral vascular disease and initial surgical treatment of AMI were protective. In contrast, the administration of antibiotics or anticoagulants was not associated with improved survival. To our knowledge, this is the first multicenter series of ICU patients with AMI that is available in the literature. In addition, we provide a score predictive of

ICU mortality in these patients, which may assist in informing patients and family or be used as part of the medical decision-making process.

The ICU mortality rate of ICU patients with AMI that we found (58 %) can only be compared to rates reported in other settings. Previously reported operative mortality of AMI ranged from 26 to 72 % with a pooled mortality rate of 47 % (95 % CI 40–54 %) [2]. However, this series did not specifically include ICU patients. The authors stated that the mortality rate for missed mesenteric ischemia that did not undergo surgery was close to 100 % [2]. In our study, 14 % of patients who did not undergo

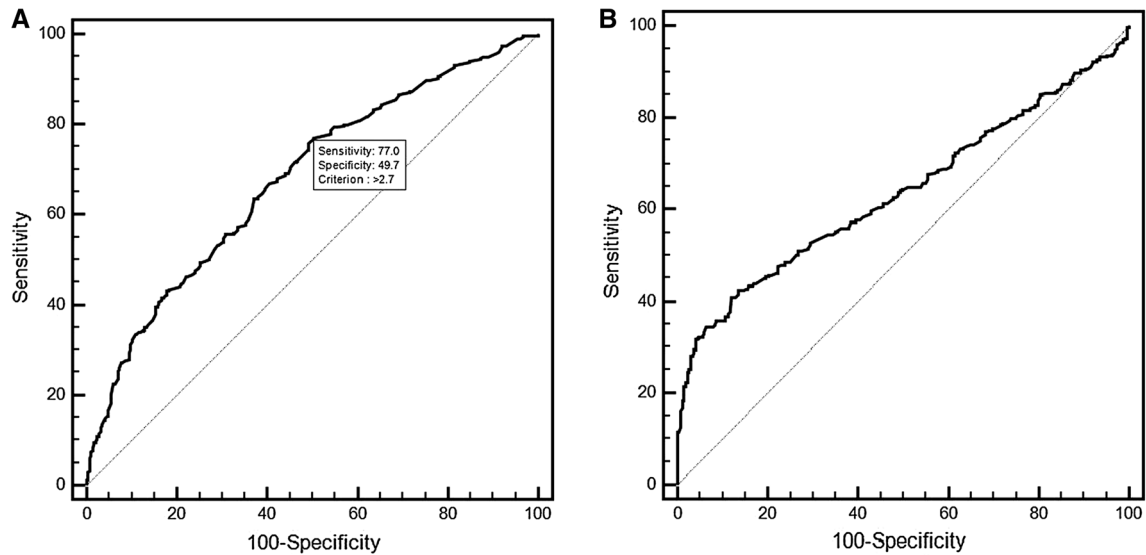


Fig. 1 Intensive care unit (ICU) mortality: receiver operating characteristics curves of **a** plasma lactate concentration at diagnosis and **b** change of plasma lactate concentration between diagnosis and 24 h

surgery survived during their ICU stay. This is probably related to nonocclusive forms of AMI. Similarly, the protection conferred by a prior history of peripheral vascular disease is also probably related to the type of AMI. In such patients, one can speculate that the disease was related to progressive thrombosis, allowing the development of important collaterals [1].

Several independent factors of mortality and protective factors have already been reported. As elsewhere [7–9], we confirmed that advanced age is an independent risk factor of mortality. Initial surgical management of AMI, i.e., performed within the first 24 h of AMI diagnosis, was associated with improved outcomes. Surgery for AMI was performed in 86 % of survivors and 71 % of nonsurvivors, resection representing 57 % of procedures. This finding is in line with previous studies showing that delay in surgery was associated with impaired outcomes [1–3]. In contrast, in the entire cohort, the time elapsed from ICU admission to AMI diagnosis was not associated with mortality rate.

Plasma lactate concentrations can successfully predict the outcomes of AMI in ICU patients. The best level for prediction of ICU death was 2.7 mmol/l. However, even if an increased plasma lactate concentration was an independent factor of mortality, the performance of plasma lactate appears disappointing. One should note that the plasma lactate concentrations remained under 2 mmol/l in 16 % of nonsurvivors. Therefore, normal plasma lactate concentrations cannot exclude the diagnosis of AMI and should not be taken into account in the diagnostic process. Nor did lactate variations over time have any added value, although we observed a trend in plasma concentration decrease from diagnosis to 24 h in patients undergoing

surgery and increase in those who did not undergo surgery. Finally, as a result of the retrospective observational design of the study, we could not measure D-lactate, which may be useful [1, 10].

Although univariate analysis showed that the rates of individual organ failures were higher in the nonsurvivors than in the survivors, in line with previous reports of liver and renal failure associated with poor outcomes in AMI [2], multivariate analysis did not confirm any one organ failure as an independent factor. However, the cumulative number of organ failures strongly impacted the outcomes. The SOFA score was higher in the nonsurvivors than in the survivors, which has not been reported elsewhere since it is a score for predicting outcomes of ICU patients only [11]. One should note that the use of this score increases the risk of re-analyzing previously utilized data in various abstracted forms. We then established a composite score including both age and SOFA score for facilitating the prediction of outcomes at the bedside. Of note, in our study heart failure was defined as the inotrope requirement or a central venous oxygen saturation below 70 %. Since central venous oxygen saturation depends on cardiac output, oxygen consumption, hemoglobin level, and arterial oxygen saturation, our definition supposed that patients were adequately resuscitated regarding preload, hemoglobin level, and arterial oxygen saturation [12]. Heart failure, shock, and vasopressor can generate the conditions for developing nonocclusive mesenteric ischemia [1]. Finally, the rate of enteral nutrition was higher in survivors than in nonsurvivors, supporting once again the use of this route in the ICU patients [13].

Several variables commonly thought to influence outcome in the ICU did not differ between survivors and

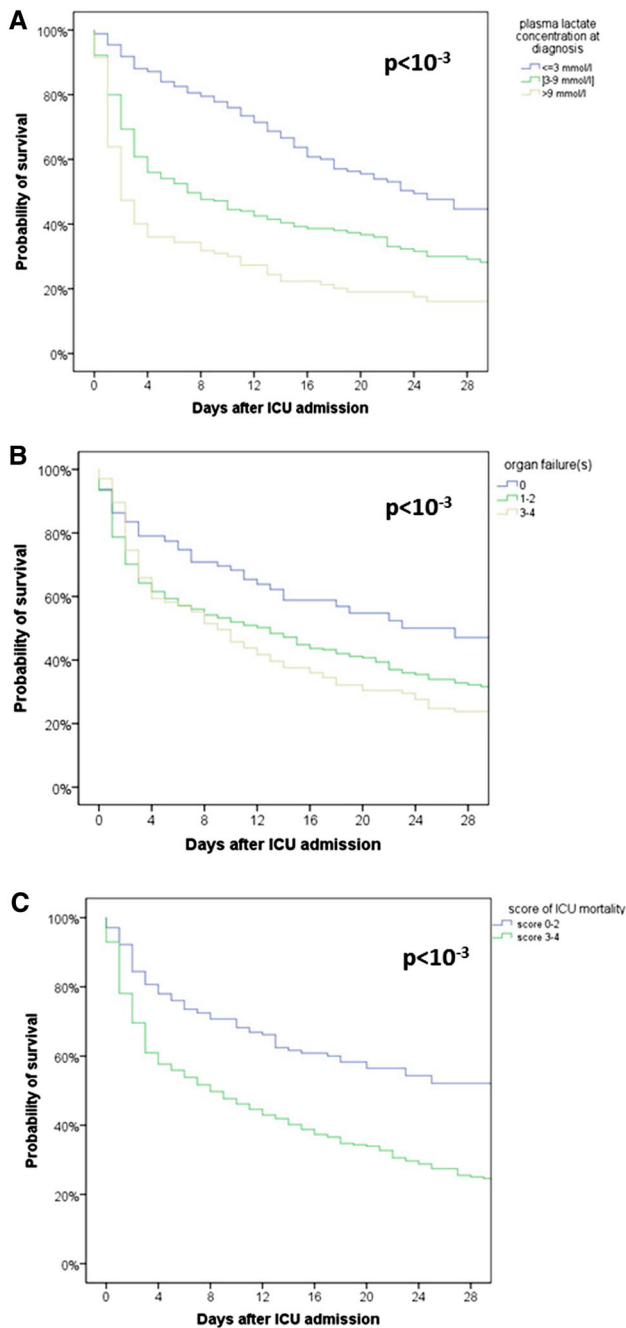


Fig. 2 Probabilities of intensive care unit (ICU) survival according to **a** the plasma lactate concentration at diagnosis, **b** the number of organ failures, and **c** the score of ICU mortality

nonsurvivors. **Antibiotics** were used in 79 % of patients with AMI, including 82 % of ICU survivors and 77 % of ICU nonsurvivors. Interestingly, multivariate analysis **did not show significant difference in terms of mortality**. While such data cannot serve to decide whether or not antibiotics should be administered in patients with AMI, they raise questions as to their systematic use [14]. Use of

vasopressors both before and after the diagnosis of AMI was more frequent in ICU nonsurvivors than in survivors. Vasopressor use in itself was not identified as an independent factor in the multivariate analysis, although it may play a role since it is taken into account in the SOFA score, which was an independent factor. Before the diagnosis of AMI, anticoagulants were used in 51 % of patients. This finding underlines that it is not reasonable to exclude this diagnosis in patients on anticoagulant therapy. In terms of mortality, no difference was observed between survivors and nonsurvivors. In contrast, after AMI diagnosis, anticoagulants were used in 91 % of survivors and 58 % of nonsurvivors. However, the use of anticoagulants was not an independent protective factor for mortality.

In our study, CT scan, surgery, and GI endoscopy were performed to confirm AMI in 58, 27, and 15 % of cases. CT scan findings were used to diagnose AMI in 63 % of survivors and 54 % of nonsurvivors. The CT scan findings of AMI depend on its origin, bowel perfusion status, and the degree of ischemia [15]. In our database, we did not collect CT scan features. The AMI was diagnosed during surgery in 21 % of survivors and 31 % of nonsurvivors. GI endoscopy led to diagnoses only of ischemic colitis. For unclear reasons, the outcome seemed impaired when AMI was diagnosed during surgery [16]. That might reflect a difference in the severity of patients, since this finding was not confirmed in the multivariate analysis.

We have to acknowledge several study limitations. As the data were retrospectively collected, we cannot determine the actual causes of death. Specifically, we did not collect data on the do not resuscitate orders, which were probably frequent in this population. The type of AMI was poorly reported, although this feature may be of interest in terms of outcomes as suggested by our data. We could not discriminate AMI due to arterial occlusions from AMI due to venous occlusions; however, this difference changes the management of patients. In addition, we did not collect data on several confounding factors such as history of hypertension, stroke, and coronary artery disease. Nor did we seek clinical or other features that had given rise to the suspected diagnosis of AMI. For instance, our data cannot discriminate if atrial fibrillation was an acute event or a chronic disease. Likewise, we did not collect on other relevant variables such as blood pressure or duration of hypotension although they are included to some degree in the SOFA score. Finally, we did not determine the delay between AMI diagnosis and surgery although surgical timing is probably one of the critical end-points in patients with AMI as it was reported elsewhere as an independent risk factor of death [1, 2, 16]. However, indirectly and only as a trend, we showed that plasma lactate concentration tended to increase in the patients who did not undergo surgery, whereas a decrease was observed in those undergoing surgery. Finally, our

Table 2 Treatments of patients with acute mesenteric ischemia according to their outcomes in intensive care unit

	MD	Total (n = 780)	Survivors (n = 326)	Nonsurvivors (n = 454)	p
Management at diagnosis					
Initial surgery (%)					
No	0	23	14	29	0.001
Yes		77	86	71	
Type of surgery					
Resection	0	442	229	213	
Bypass		22	17	5	
Thrombectomy		2	2	0	
CT scan (%)					
Yes	0	1.9	1.8	2.0	0.147
Antibiotic at diagnosis (%)	0	79	82	77	
Antibiotic duration (days)					
619 patients, mean ± SD		6.5 ± 5.8	8.7 ± 4.9	4.8 ± 6.0	0.001
Mechanical ventilation (days)					
702 patients, mean ± SD		8.8 ± 11.8	10.3 ± 12.9	7.9 ± 11.0	0.012
Before diagnosis					
Vasopressor (%)	0	44	29	55	0.001
Anticoagulants (%)	2	51	49	52	0.512
Mechanical ventilation (days)					
319 patients, mean ± SD		5.9 ± 8.7	5.9 ± 10.2	5.9 ± 8.1	0.97
Enteral nutrition (%)	7	49	54	46	0.021
Parenteral nutrition (%)	7	12	9	15	0.017
After diagnosis					
Vasopressor (%)	22	79	73	83	0.001
Anticoagulants (%)	6	72	91	58	0.001
Mechanical ventilation (days)					
671 patients, mean ± SD		6.6 ± 9.4	8.6 ± 9.7	5.1 ± 8.9	0.001
Enteral nutrition (%)	8	37	65	16	0.001
Parenteral nutrition (%)	7	45	67	29	0.001

CT computed tomography, MD missing data, SD standard deviation

Table 3 Risk factors of ICU mortality

	OR	95 % CI	p
Age at admission (class: 10 years)	1.27	1.11–1.46	<0.001
History of cancer (ref: no)	1.56	0.97–2.49	0.065
History of peripheral vascular disease (ref: no)	0.56	0.38–0.82	0.003
Shock in the preceding 10 days (ref: no) ^a	1.01	0.69–1.49	0.948
SOFA at diagnosis (class: 4 points)	2.08	1.73–2.50	<0.001
Lactate at diagnosis (ref: ≤2.7 mmol/l) ^b	2.36	1.52–3.66	<0.001
Antibiotic at diagnosis (ref: no)	0.71	0.44–1.14	0.108
Initial surgical treatment (ref: no)	0.27	0.16–0.43	<0.001
Time between ICU admission and diagnosis	1.01	0.99–1.04	0.297

OR odd ratio, 95 % CI 95 % confidence interval, p p value of the logistic regression, SOFA sequential organ failure assessment

^a Before intensive care unit (ICU) admission

^b Optimal cutoff value of the receiver operating characteristics

data cannot serve to determine the incidence of AMI among ICU patients.

In conclusion, our retrospective analysis of 780 ICU patients with AMI shows that the ICU mortality of patients with AMI was high, around 58 %. Increasing age, SOFA score at diagnosis, and plasma lactate concentrations above 2.7 mmol/l at diagnosis were associated with increased ICU death rate, whereas a prior history of

peripheral vascular disease and an initial surgical treatment were associated with positive outcomes. A composite score integrating both age and SOFA score was established in order to facilitate the prediction of outcomes in ICU.

Conflicts of interest The authors have no conflict of interest to disclose related to this topic.

Appendix: List of investigators

Pierre Asfar, Johan Auchabie (Hôpital Universitaire d'Angers), Gaston Grossmith (Centre Hospitalier Edmond Garcin, Aubagne), Pierre Courant (Centre Hospitalier d'Avignon), Jean-Luc Fellahi (Centre Hospitalo-Universitaire de Caen), Mélanie Tari, Bertrand Souweine (Centre Hospitalier de Clermont Ferrand), Pierre Visintini (Centre Hospitalier Interrégional des Alpes du Sud, Gap), Tarek Sharshar (Hôpital Raymond Poincaré, Montigny le Bretonneux), Vincent Piriou (Hospices Civils de Lyon), Djamel Mokart (Institut Paoli-Calmettes, Marseille), Sandrine Wiramus, Jacques Albanèse (Hôpital la Conception, Marseille), Alexandre Marillier, Nicolas Bruder (Hôpital la Timone, Marseille),

Sami Hraiech, Laurent Papazian (Réanimation DRIS, Hôpital Nord, Marseille), Claire Contargyris (Hôpital Laveran, Marseille), Xavier Capdevila (Hôpital Lapeyronie, Montpellier), Julien Darmian (CHU Nancy Hôpital Central), Loubna Elotmani (Hôpital Carremeau, Nîmes), Thierry Boulain (Hôpital de la Source, Orléans), Philippe Montravers (Hôpital Bichat, Paris), Jean-Paul Mira, Frédéric Pene (Hôpital Cochin, Paris), Olivier Langeron (Hôpital la Pitié Salpêtrière, Paris), Matthieu Legrand (Hôpital Saint Louis, Paris), Dorothé Balayn, Sabrina Seguin (CHU de Poitiers), Ali Mofredj (Centre Hospitalier de Salon), Marie-Charlotte Vogler, Serge Molliex (CHU Saint Etienne), Olivier Fourcade, Thomas Geeraerts (CHU Toulouse).

References

1. Oldenburg WA, Lau LL, Rodenberg TJ, Edmonds HJ, Burger CD (2004) Acute mesenteric ischemia: a clinical review. *Arch Intern Med* 164:1054–1062
2. Cudnik MT, Darbha S, Jones J, Macedo J, Stockton SW, Hiestand BC (2013) The diagnosis of acute mesenteric ischemia: a systematic review and meta-analysis. *Acad Emerg Med* 20:1087–1100
3. Gupta PK, Natarajan B, Gupta H, Fang X, Fitzgibbons RJ Jr (2011) Morbidity and mortality after bowel resection for acute mesenteric ischemia. *Surgery* 150:779–787
4. Vincent JL (2006) Organ dysfunction in patients with severe sepsis. *Surg Infect (Larchmt)* 7(Suppl 2):S69–S72
5. Therneau TM, Atkinson EJ (2000) An introduction to recursive partitioning using the RPART routines. Technical report 61. Mayo Clinic, Rochester
6. Roch A, Hraiech S, Masson E, Grisoli D, Forel JM, Boucekine M, Morera P, Guervilly C, Adda M, Dizier S, Toesca R, Collart F, Papazian L (2014) Outcome of acute respiratory distress syndrome patients treated with extracorporeal membrane oxygenation and brought to a referral center. *Intensive Care Med* 40:74–83
7. Haga Y, Odo M, Homma M, Komiya K, Takeda K, Koike S, Takahashi T, Hiraka K, Yamashita H, Tanakaya K (2009) New prediction rule for mortality in acute mesenteric ischemia. *Digestion* 80:104–111
8. Aliosmanoglu I, Gul M, Kapan M, Arikanoğlu Z, Taskesen F, Basol O, Aldemir M (2013) Risk factors effecting mortality in acute mesenteric ischemia and mortality rates: a single center experience. *Int Surg* 98:76–81
9. Acosta-Merida MA, Marchena-Gomez J, Hemmersbach-Miller M, Roque-Castellano C, Hernandez-Romero JM (2006) Identification of risk factors for perioperative mortality in acute mesenteric ischemia. *World J Surg* 30:1579–1585
10. Vincent JL, de Mendonça A, Cantraine F, Moreno R, Takala J, Suter PM, Sprung CL, Colardyn F, Blecher S (1998) Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on “sepsis-related problems” of the European Society of Intensive Care Medicine. *Crit Care Med* 26:1793–1800
11. Demir IE, Ceyhan GO, Friess H (2012) Beyond lactate: is there a role for serum lactate measurement in diagnosing acute mesenteric ischemia? *Dig Surg* 29:226–235
12. Reinhart K, Kuhn HJ, Hartog C, Bredle DL (2004) Continuous central venous and pulmonary artery oxygen saturation monitoring in the critically ill. *Intensive Care Med* 30:1572–1578
13. Casaer MP, Van den Berghe G (2014) Nutrition in the acute phase of critical illness. *N Engl J Med* 370:1227–1236
14. Berland T, Oldenburg WA (2008) Acute mesenteric ischemia. *Curr Gastroenterol Rep* 10:341–346
15. Lee SS, Park SH (2013) Computed tomography evaluation of gastrointestinal bleeding and acute mesenteric ischemia. *Radiol Clin N Am* 51:29–43
16. Acosta S, Björck M (2014) Modern treatment of acute mesenteric ischaemia. *Br J Surg* 101:e100–e108