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Epidemiology and complications of anaesthesia in the French centres that participated to NECTARINE: A secondary analysis

Short Title: Results of the NECTARINE trial in France

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SD: study conception, data collection, data analysis, interpretation of results, drafting and correcting the manuscript and approved the final version of the manuscript.

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- a) What is already known: The perioperative management of neonates and infants is a highly specialised activity carrying an increased risk of morbidity and mortality.
- b) What this article adds: The current study describes the epidemiologic and perioperative data of the population of infants anaesthetised in the French centres that participated to NECTARINE. The French data contributed to 14.1% the NECTARINE study data set. There were no major differences in mortality and morbidity in the European and French cohorts. Awake-regional anaesthesia was more often used but invasive arterial blood pressure monitoring was less frequently used in the French centres. Most of the thresholds used to react to a critical event did not meet the published standards.
- c) Implications for translation: Educational effort to disseminate recent clinical and basic sciences evidence to improve the perioperative management of infants must be considered.

Abstract

Introduction: Neonatal and infant anaesthesia are associated with a high risk of perioperative complications. The aim of the current study was to describe those risks in France using the French data from the NECTARINE study.

Material and Methods: Data from the French centres that participated to the NECTARINE study were analysed. The primary goal of the study was the description of patients' characteristics, procedures and perioperative management and their comparison with the results of the European NECTARINE study. Secondary outcomes were the description of major perioperative complications and death.

Results: Overall, 926 procedures collected in 15 centres (all teaching hospitals) were analysed. Comparison between the French and European NECTARINE cohorts found few differences related to patients' characteristics and procedures. The rate of interventions for critical events (respiratory, haemodynamic, and metabolic) was similar between the two cohorts. Near-infrared spectroscopy monitoring was used in 12% of procedures. Nearly none of the thresholds for these interventions met the published standards. By day 30, complications (respiratory, haemodynamic, metabolic, renal, and liver failure) and death were observed in 14.4% [95% CI 11.6 – 16.4] % and 1.8% [95 % CI 1.1 – 2.9] of cases, respectively.

Discussion: Although the health status of the patients in the French cohort was less severe, procedures, management and postoperative complications and mortality rates were similar to the European cohort. However, thresholds for interventions were often inadequate in both cohorts. Efforts should be undertaken to improve the knowledge and use of new monitoring devices in this population.

Introduction

Published evidence indicates that a high proportion of neonates and infants undergoing anaesthesia might present perioperative complications with an increased risk of immediate and delayed morbidity and mortality (1-4). Because of their organ immaturity and increased sensitivity to anaesthetics agents, these patients are at high risk for haemodynamic, respiratory, and metabolic compromises (5-7). In addition, the management of these patients requires a specific training, appropriate skills and human resources investment in a context of shortage (1, 2, 8).

Data concerning the perioperative management of neonates and infants are scarce. To date, only a few studies have tried to summarise their postoperative prognosis and the factors associated with their morbidity and mortality (1, 3, 4, 8). The NECTARINE study (9) represents with this regard, a great step forward in describing the perioperative management of this specific population and the risk factors associated with the occurrence of death or complications. However, its results exhibit a high heterogeneity that is probably the result, as was the case for the previous APRICOT study, of differences in national practices (1).

The primary aim of the current study was to describe patients' characteristics, procedures and management of neonates and infants included in the NECTARINE study in France and to compare them with the European cohort (French data included). The secondary aim was to compare the incidence of major complications and death 30 and 90 days after anaesthesia in both cohorts.

Material and Methods

Study design

The study design has been described in detail in the original publication (9). The study consisted in the prospective collection of perioperative data from children recruited in 261 centres across 39 European countries during a consecutive 12-week period freely chosen by each centre, between the 1st of March 2016, and the 31st of January 2017. Regarding France, the study was nationally approved by an IRB (CPP Sud Méditerranée # 2016-A00169-42). Given the observational nature of the study, guardians' and patients' consent was waived by the IRB). Data were collected on an online electronic database approved by the French regulatory office for the protection of privacy (CNIL). The current study used all data collected in the French participating centres after approval by the Steering Committee of the NECTARINE study and the French national coordinators (AL and CD).

The study included all neonates and infants with a postmenstrual age < 60 weeks at inclusion (time of first anaesthesia). The details of the data collected are described in the original NECTARINE study (9). In summary, data consisted in: maternal and child's characteristics before surgery (or procedure), preoperative location, surgery and/or procedure performed, management of the perioperative period, the occurrence of any preselected critical event (haemodynamic, respiratory, metabolic including temperature variations), monitoring used to detect those critical events, interventions to correct those critical events and parameter thresholds (absolute values or percentage variations) that lead to these interventions. The study also collected data on postoperative complications and deaths at day 30 and 90 after surgery or procedure.

The preselected critical events were defined in the original NECTARINE study as follows: (a) decrease in SpO₂, PaO₂, or both (intervention to improve oxygenation); (b) increased or decreased in end-tidal carbon dioxide (ETCO₂), arterial/venous blood CO₂ (intervention to improve alveolar ventilation), or both; (c) decrease in systolic or mean arterial blood pressure; (d) change in heart rate, ECG rhythm disturbances, or both, resulting in cardiovascular instability; (e) absolute values or relative decrease in cerebral oxygenation when near-infrared spectroscopy (NIRS) was part of clinical monitoring; (f) abnormal blood glucose, plasma sodium (Na), or both; (g) low haemoglobin values (need transfusion of packed red cells); (h) hypo- or hyperthermia and associated core body temperature .

Data extraction

The analysis of data was focused on: the demographic and perinatal characteristics; any history of apnoea, intraventricular haemorrhage, patent ductus arteriosus, previous ECMO support (patient with this procedure performed previous to surgery) (9) or previous surgery; the preoperative location (home, intensive care, other hospital and wards); the presence of any respiratory, cardiovascular, neurological, metabolic or renal preoperative compromise; the ASA health status (ASAhs); the nature of surgical and non-surgical procedures; the management of anaesthesia (including mode of induction and drugs used); monitoring during anaesthesia : standard (ECG, SpO₂, non-invasive blood pressure and temperature) arterial line, central venous pressure and near-infrared spectroscopy monitoring (NIRS); the ventilation management; the occurrence of any of the preselected critical event and its management, the location of postoperative care at day 30 after the procedure; the presence of any respiratory, cardiovascular, neurological, renal or liver complication at day 30 and the incidence of death 30 and 90 days after surgery or

procedure. The details of the complications reported in the electronic case report form are available in **Supplementary file 1**.

Statistical analysis

We choose to compare the French data (926 procedures in 880 patients) with the whole NECTARINE cohort (6542 procedures in 5609 patients) as available in the original publication (9) in the same way as in the previous publication on the French data in APRICOT (8). We thought that comparing the French data with the whole NECTARINE cohort minus the French data (5616 procedures in 4729 patients) would be less appropriate to evaluate the performance of the French participating centres even if other countries used the later model to study their APRICOT data (10). Consequently, no statistical comparison was performed between the French and European data. We took nevertheless great care to check each item to avoid any misinterpretation of the results if the French contribution was either much lower (*e.g.*, MRI cases) or greater (*e.g.*, neonates on ECMO) than expected when looking at the European data. Descriptive analysis used percentages, mean and standard deviation or median and ranges, as appropriate.

To allow comparisons between the French and European results, analysis of the data is displayed according to the corrected ages at the time of surgery (as in the original publication): < 28 weeks, 29 to 31 weeks, 32 to 36 weeks, 37 to 40 weeks, 41 to 44 weeks, 45 to 60 weeks, and total cohort.

Results

Overall, 15 centres (all teaching hospitals) in France included 926 procedures in 880 patients. This represents 15.6% and 14.1% of the total patients and procedures included in the European cohort, respectively. All procedures were included in the final analysis of the French cohort.

Description of patients and procedures in the French NECTARINE cohort in comparison to the European NECTARINE data

Characteristics of patients are displayed in **Table 1**. Mean gestational age and weight at birth were 36 ± 4 weeks and 2668 ± 943 grams, respectively, similarly to the European cohort. The incidence of congenital abnormalities was similar in the two cohorts except for the proportion of cardiac malformations that was higher in the European cohort in comparison to the French one (12.7% versus 4.9%, respectively). Other conditions, namely: history of apnoea or respiratory support, intraventricular haemorrhage, previous patent ductus arteriosus and surgery were also more frequent in the European cohort. In addition, the proportion of patients on ventilator support at the time of anaesthesia was greater in the European cohort. This translates in the ASAhs with a greater proportion of patients exhibiting an ASAhs III to V in the European cohort. However, more patients were on ECMO before surgery in the French cohort: 13 out of a total of 19 in Europe.

The details of the procedures performed and their characteristics are displayed in **Table 2**. Four hundred and thirty-two (46.7%) of the surgical procedures were elective. One hundred sixteen (13.2%) patients in the French cohort went under anaesthesia more than once in comparison to 1631 (24.9%) in the European cohort. Gastro-intestinal and

oesophageal surgery were the most frequent surgeries. Cardiac surgery was more frequent in the European cohort (8.4%) in comparison to the French one (2.4%). Non-surgical procedures were also more frequent in the European cohort, with anaesthesia or sedation for MRI being largely more frequent in the European cohort (6.1% *versus* 25.4% in the French and European cohorts, respectively).

The detail of perioperative management in the French cohort is also displayed in **Table 2**. At least one senior anaesthesiologist was present in 80.5% of the procedures and an anaesthetic nurse was present in 96.3% of them. Standard monitoring was used in 100% of cases and a NIRS monitor was used in only 111 procedures (12%). Those results were similar to the European cohort. Invasive arterial monitoring was used less frequently in the French cohort: 1.8 *vs.* 13.6% of the cases in Europe. Awake-regional anaesthesia was performed in 95 patients (10.3% of the French cohort *vs.* 2.1% of the complete European cohort) while all others were managed with either general anaesthesia or combined general and regional anaesthesia. Induction of anaesthesia was most frequently performed using inhaled anaesthetics agents. Opioids were administered for induction or maintenance of anaesthesia in 57.6% and 45.1% of cases, respectively. In case of intravenous induction, propofol was used in 357 cases (43%) and ketamine in 155 (18.6%). Atropine was administered during induction in 91 cases (9.1%). Neuromuscular blocking (NMB) agents were used during 314 procedures (37.8%) and were antagonised in only 11 cases at the end of the procedure (3.5% of patients in which a NMB was administered). Endotracheal intubation and controlled ventilation with an oxygen-air mixture was the most frequent ventilatory management and was similar in both cohorts.

Description of critical events and interventions

The number of interventions was too small to provide precise data according to the range of postmenstrual ages (as performed in the original publication of the study (9)). Comparisons of descriptive data are displayed in **Table 3**. Major differences between the French and European cohorts were: a greater proportion of intervention for a decrease of mean blood pressure (despite a similar threshold value in both two cohorts); a higher mean threshold for intervention in case of a decreased heart rate in the French cohort in comparison to the European one (98 bpm *versus* 81 bpm, respectively); a lower mean threshold for an increased end-tidal CO₂ value in the French cohort in comparison to the European one (45.6 mmHg *versus* 59.2 mmHg) and a higher mean threshold for intervention in case of a decrease in NIRS value (52 *versus* 45) but with a similar mean threshold for the relative change of NIRS in comparison to its baseline value (around – 30% on average). Finally, ephedrine was the vasoactive drug the most frequently used to treat haemodynamic instability (a decreased blood pressure or NIRS value).

Description of perioperative complications and death in the French NECTARINE cohort and their comparison with the European cohort

A total of 790 patients (89.8%) could be followed up at 30 days (*versus* 5510, or 93.3%, in the European cohort). Mortality at day 30 was 1.8% [95% CI 1.1 – 2.9] % in the French cohort and 1.9 % in the European one (Table 4). Complications occurred in 14.4% [95% CI 11.6 – 16] of cases in the French cohort in comparison to 17% [95 % CI: 16 – 18] in the European one. Details of those complications are displayed in **Table 4**. Except for surgical

complications that were more frequent in the European cohort, the other rates of complications were similar between the two cohorts.

Discussion

The current study summarises the data from the French centres that participated to the NECTARINE study and allows comparing them to the European data. It gives a snapshot of the practice of anaesthesia in neonates and infants < 60 weeks postmenstrual age in the 15 French facilities specialised in paediatric anaesthesia that participated to the study and a detailed outcome 30 days after anaesthesia.

Comparing the French and European cohorts revealed some differences between the patients' characteristics. The population included in the French cohort presented less severe conditions in comparison with the overall European cohort: less congenital abnormalities and a lower proportion of patients with a history of major organ failures. In addition, cardiac surgery was underrepresented in the French cohort in comparison to the European cohort. This might also account for the difference in health status between patients of the two cohorts given the consequences of congenital cardiac abnormalities that need to be palliated or corrected in the neonatal period. This translates into a greater proportion of patients exhibiting an ASAhs I to III in the French cohort in comparison to the European one (72.2 % *versus* 59.7 %, respectively). A history of ECMO support was more frequent in the French cohort as 13 out of the 19 patients of the European cohort were operated in France. This might result from a recruitment bias or increased availability or experience with neonatal ECMO in France. Finally, anaesthesia for MRI was underrepresented in the French cohort, which raises the question of differences in

management strategies between European countries. For example, it is possible that MRI in neonates and infants are performed without any intervention of anaesthesiologists in France (pharmacologic or non-pharmacologic sedation by radiologists or neonatologists). Otherwise, difference in indications for neonatal MRI within European countries might also account for this difference.

Concerning anaesthesia management, in France most procedures were performed by a senior anaesthesiologist with the help, in most cases, of an anaesthetic nurse. This represents a major quality indicator given that the presence of an experienced physician and an anaesthetic nurse has been previously found as a factor associated with a decrease in perioperative complications during paediatric anaesthesia (1, 8, 11). Concerning the anaesthetic technique and drugs, awake-regional anaesthesia alone was much more frequently used in the French cohort. This probably reflects a longstanding tradition of using awake spinal anaesthesia for herniorrhaphy in neonates and ex premature infants in France, and a greater proportion of inguinal herniorrhaphies performed in this cohort: 288 (34.7% of all surgical procedures) cases in France on a total of 1408 (27% of all surgical procedures) in Europe. Inhaled induction was the most frequent technique. Although, propofol was the most frequently used intravenous agent used for induction, ketamine was also used. Interestingly, atropine was administered in 9.1% of inductions. This probably indicates that some physicians continue to administer it systematically. Airways were almost always managed using a tracheal tube and ventilation used the controlled mode.

Concerning adverse events, the French cohort thresholds for interventions were similar to the European one except for a decreasing of heart rate (recommended value for intervention < 90 bpm) (9, 11) and absolute NIRS values (recommended value for intervention < 60%) (9, 12, 13) that were higher for the French cohort. However, as clearly

discussed in the NECTARINE original article, values of arterial pressure triggering interventions were low. Considering variations of mean arterial pressure (in comparison to the baseline values), these thresholds were on average 42% below baseline in the French cohort. These values were below the published data showing a possible association with cerebral desaturation (20% below baseline) in small infants (13-15). In addition, NIRS monitoring that might help identifying cerebral haemodynamic compromise was used in only 12% of cases with a relative triggering value for intervention of 30% below baseline while recommendations at that time set this threshold trigger to 20% (12, 13, 16, 17). However, one must keep in mind that at the time of the NECTARINE study, many centres in France and Europe were not (yet) equipped with NIRS and that evidences for the use of NIRS were not as strong as today (17). As described for the whole European cohort, the threshold value for a reaction to peripheral arterial oxygen desaturation was < 85% in more than half of cases; while recommended values for intervention are usually 95 to 90% (9, 18). This could be a consequence of using the lowest FiO₂ possible in this population to prevent retinopathy of prematurity. Finally, interventions for hypothermia were triggered when values were 35 °C while a greater value might help more rapid restoration of normothermia. In France, ephedrine was the most used vasoactive drug for the correction of hypotension. This could indicate a switch of the treatment strategy of systemic hypotension from increasing the heart rate to improving volaemia (venous return) (19, 20).

Concerning the complications, and despite a better average preoperative health status of the French patients, the incidence of deaths and complications at day 30 were similar in both the two cohorts. This could be due to intercurrent events occurring between the procedure and the time of assessment, especially when patients are admitted in the intensive care. Differences between the two cohorts concerning postoperative complications

were obvious for the surgical ones. This might be attributable to the higher proportion of cardiac surgery in the European cohort as it is usually associated with a higher rate of postoperative medical and surgical complications.

The current study presents the same limitations as the original publication. Moreover, the current cohort was national and included patients whose preoperative health status was less severe than the European one. Unfortunately, the number of adverse events and interventions was too low to allow describing the interventions according to postmenstrual age categories. Moreover, the data collected are limited to the number and case mix of the centres that participated: for example, some French paediatric cardiac surgery centres did not participate to NECTARINE. In addition, incident reporting was voluntary: one can only hypothesise that all critical events were reported. One should also emphasise that no information was available, by study design, about the preventive measures taken to avoid critical events such as adapting ventilation or FiO_2 , or preemptive volume loading. Finally, the large variability and imprecision of the monitoring (SpO_2 , EtCO_2 , blood pressure and NIRS) in this population might also result in some bias as their values might have been (initially) considered as artefactual or unreliable by the team in charge.

Nevertheless, our study sheds the light on the importance of education and more standardised practices in the field of neonatal and infant anaesthesia. This is not only supported by the analysis of both cohorts but also by previous studies showing the increased incidence of complications and mortality associated with the surgery and/or anaesthesia in neonates and infants (3, 4, 11). All participating centres were indeed teaching facilities, and one would expect that a more rigorous observance of the theoretical target values (at least for SpO_2 , EtCO_2 , blood glucose, NIRS and temperature) for interventions would have been observed. Consequently, the current results should be considered as a warning toward a

more active diffusion of current knowledge about the optimal perioperative management of neonates and small infants. Although evidence is lacking about any association between NIRS monitoring and perioperative outcome in non-cardiac surgery (12, 16), the lack of reliable haemodynamic monitoring in neonates and infants and the relation between cerebral saturation and cerebral autoregulation makes NIRS devices as valuable – or at least helping – tool to monitor haemodynamics in this population (6, 17). Consequently, facilities should be sensibilised to these facts and encouraged to be equipped with NIRS devices for use in at least all-neonatal cases.

In conclusion, this study described the perioperative management of neonates and infants < 60 weeks of postmenstrual age in the French centres that participated to NECTARINE. Results concerning the adverse events, their management and outcomes indicate that efforts should be undertaken to improve the knowledge and use of recent standards of care and new monitoring devices in this population.

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Table 1: Patients' and surgery characteristics

Factor	French cohort (n = 880)	European Cohort (n = 5609)
Gestational age at birth (weeks)	36 ± 4	36 ± 4
Weight at birth (g)	2668 ± 943	2730 ± 984
Male gender	592 (67.3 %)	3670 (65.4 %)
Mode of delivery: caesarean	247 (28.1 %)	2253 (40.2 %)
APGAR at 5 minutes	10 ± 9	9 ± 10
Congenital abnormalities	282 (30.5 %)	2456 (43.8 %)
- Myopathy	6 (0.7 %)	#
- Heart diseases	38 (4.3 %)	714 (12.7 %)
- Metabolic	10 (1.1 %)	84 (1.5 %)
- Chromosomopathy	14 (1.6 %)	131 (2.3 %)
- Others	208 (23.6 %)	1795 (32 %)
History of apnoea/respiratory support	250 (28.4 %)	4015 (38.6 %)
Intraventricular haemorrhage	28 (3.2 %)	463 (7.1 %)
History of ECMO support	1 (0.1 %)	62 (0.9 %)
History of PDA	79 (9 %)	1219 (18.6 %)
History of previous surgery	116 (13.2 %)	1631 (24.9 %)
Post-conceptual age at inclusion (weeks)	44.7 ± 6.5; 44 [40, 49] **	57 [22, 97] **
- < 28 weeks	4 (0.5 %)	68 (1.2 %)
- 28-31 weeks	19 (2.2 %)	115 (2 %)
- 32-36 weeks	49 (5.6 %)	507 (9 %)
- 37-40 weeks	153 (17.4 %)	1309 (23.3 %)
- 41-44 weeks	231 (26.3 %)	1406 (25 %)
- 45-60 weeks	424 (48.2 %)	3137 (55.9 %)
Weight at inclusion (kg)	4 ± 1.3	4.1 ± 1.5
- < 28 weeks	##	0.8 ± 0.2
- 28-31 weeks	1.3 ± 0.8	1.3 ± 0.5
- 32-36 weeks	2.2 ± 0.6	2.2 ± 0.6
- 37-40 weeks	3 ± 0.5	3.3 ± 0.7
- 41-44 weeks	3.6 ± 0.6	3.7 ± 0.7
- 45-60 weeks	5 ± 1	5.2 ± 1.3
Admission of child at time of inclusion		
- Home/ward	634 (68.5 %)	4226 (64.6 %)
- Another hospital	52 (5.6 %)	504 (7.7 %)
- ICU	240 (25.9 %)	1812 (27.7 %)
Breathing conditions *		
- Spontaneous no oxygen	787 (85 %)	5608 (77.5 %)
- Spontaneous on oxygen	25 (2.7 %)	409 (6.3 %)
- Non-invasive ventilation	16 (1.7 %)	173 (2.6 %)
- Intubation & ventilation	105 (11.3 %)	873 (13.4 %)
- Intraoperative ECMO	13 (1.4 %)	19 (0.3 %)
Patient assessment at time of surgery *		
- Respiratory problems	137 (14.8 %)	1194 (18.3 %)
- Cardiovascular problems	102 (11 %)	1404 (21.5 %)
- Metabolic problems	99 (10.7 %)	666 (10.2 %)
- Neurological problems	37 (4 %)	813 (12.4 %)
- Renal problems	41 (4.4 %)	462 (7.1 %)
ASA health status at time of inclusion		
- I	145 (16.5 %)	757 (11.6 %)
- II	503 (57.2 %)	3148 (48.1 %)

- III	190 (21.6 %)	1923 (29.4 %)
- IV	36 (4.1 %)	670 (10.2 %)
- V	6 (0.6 %)	38 (0.6 %)

ECMO: extracorporeal membrane oxygenation, PDA: patent ductus arteriosus. * Proportions were calculated relative to the number of procedure (n = 926) given that preoperative condition might change according to each procedure. Data are expressed as mean sd or N (%) except for post-conceptual age (**) expressed in median [Q1, Q3] because original data were expressed so (9). #: data not available in the original publication of the European cohort. # #: there were no patients with a post-conceptual age at inclusion < 28 weeks in the French cohort.

Table 2: Surgery and Anaesthesia management characteristics for procedures

Factor	French cohort (n = 926)	European cohort (n = 6542)
Location of surgery operative theatre	900 (97.2 %)	6279 (96 %)
Elective/emergency		#
- Elective	432 (46.7 %)	
- Semi-emergency	329 (35.5 %)	
- Emergency	165 (17.8 %)	
Surgical procedure	830 (89.6 %)	5200 (79.5 %)
- Gastro-intestinal	622 (74.9 %)	3215 (61.8 %)
- Cardiac	20 (2.4 %)	439 (8.4 %)
- Thoracic	14 (1.7 %)	58 (1.1 %)
- Genitourinary	44 (5.3 %)	350 (6.7 %)
- Neurosurgery	21 (2.5 %)	333 (6.4 %)
- Ophthalmic	6 (0.7 %)	140 (2.7 %)
- Ear nose and throat	53 (6.4 %)	340 (6.5 %)
- Orthopaedic	44 (5.3 %)	204 (3.9 %)
- Dermatological	12 (1.4 %)	154 (3 %)
Non-surgical procedure	98 (10.6 %)	1341 (20.5 %)
- Angiography/embolisation,	5 (5.1 %)	31 (2.3 %)
- Biopsy,	9 (9.2 %)	47 (3.5 %)
- Bronchoscopy,	12 (12.2 %)	153 (11.4 %)
- Burns dressing,	1 (1 %)	3 (0.2 %)
- Cardiac lab (Percutaneous valvuloplasty, Rashkind procedure),	3 (3.1 %)	102 (7.6 %)
- CT-Scan,	0 (0 %)	40 (3 %)
- Cystoscopy/vaginoscopy	2 (2 %)	73 (5.4 %)
- Gastroenterology,	16 (16.3 %)	98 (7.3 %)
- Infiltration or punction,	4 (4.1 %)	34 (2.5 %)
- MRI (Magnetic Res Imaging),	6 (6.1 %)	340 (25.4 %)
- Ophthalmologic examination/Laser	2 (2 %)	40 (3 %)
- Pericardial or pleural drainage	1 (1 %)	14 (1 %)
- PICC line/Central venous/Broviac	27 (27.6 %)	251 (18.7 %)
- Others	10 (10.2 %)	114 (8.5 %)
Duration of surgery or procedure (minutes)	283 ± 962	#
Human resources during anaesthesia		#
- Presence of a senior anaesthesiologist	745 (80.5 %)	
- Junior anaesthesiologist	267 (28.8 %)	
- Training anaesthesiologist	363 (39.2 %)	
- Presence of an anaesthetic nurse	892 (96.3 %)	
Monitoring		#
- Standard	926 (100 %)	
- Arterial	17 (1.8 %)	898 (13.6 %)
- Central venous pressure	98 (10.6 %)	#
- Near-infrared spectroscopy	111 (12 %)	533 (8 %)
Anaesthesia		
- General	461 (49.8 %)	4391 (67.1 %)
- Regional	95 (10.3 %)	216 (3.3 %)
- General & regional	370 (40 %)	1935 (29.6 %)
Anaesthesia technique when general anaesthesia is used		#
- Inhaled induction (sevoflurane)	510 (61.4 %)	
- Intravenous only	321 (34.7 %)	
- Use of propofol for induction	357 (43 %)	
- Use of thiopental for induction	52 (6.2 %)	
- Use of ketamine for induction	155 (18.6 %)	
- Use of atropine during induction	91 (10.9 %)	
- Opioids during induction	479 (57.6 %)	
- Intraoperative neuromuscular blocking agent	314 (37.8 %)	
- Suxamethonium during induction	157 (18.9 %)	
- Maintenance Sevoflurane	713 (85.7 %)	
- Maintenance propofol	43 (5.2 %)	
- Maintenance opioids	375 (45.1 %)	
- Reversing neuromuscular blocking agent*	11 (1.3 %)	
Gas mixture during general anaesthesia		#
- Oxygen	35 (4.2 %)	
- Oxygen & N ₂ O	66 (7.9 %)	
- Oxygen & air	728 (89.7 %)	
Airway management device patients with general anaesthesia		
- None	5 (0.6 %)	
- Facemask	105 (12.7 %)	827 (12.6 %)
- Endotracheal tube	640 (77.2 %)	4624 (71.6 %)

- Endotracheal cuffed tube	420 (50.5 %)	#
- Supraglottic device	69 (8.3 %)	722 (11 %)
- Tracheostomy	1 (0.1 %)	#
Ventilation mode in patient with general anaesthesia		#
- Spontaneous	114 (13.7 %)	
- Assisted ventilation	73 (8.8 %)	
- Controlled ventilation	644 (77.5 %)	
- Level of End-expiratory pressure (cmH ₂ O)	4 ± 1	

* Percentage of those receiving neuromuscular blocking agents. Data are expressed as mean ± sd or N (%). #: data not available in the original publication of the European cohort.

Table 3: Interventions for critical events for procedures

Factor	French cohort (n = 926)	European Cohort (n = 6542)
Intervention critical events	352 (38 %)	2306 (35.2 %)
Systolic blood pressure		
- Baseline	77.6 ± 17.5	78.1 ± 17.3
- Threshold for intervention	45.7 ± 10.8	46.2 ± 9.9
- Threshold for drug administration	47.5 ± 12	#
- Number of interventions n (%)	80 (8.6 %)	673 (10.3 %)
- Number of drug administration n (%)	40 (4.3 %)	370 (5.7 %)
Mean blood pressure		
- Baseline	54.9 ± 14.5	54.8 ± 14.2
- Threshold for intervention	31.9 ± 6.7	32.5 ± 6.7
- Threshold for drug administration	32.1 ± 6.9	#
- Number of interventions n (%)	144 (15.5 %)	558 (8.5 %)
- Number of drug administrations n (%)	82 (8.8 %)	373 (5.7 %)
Drug administration for low systolic/mean blood pressure (n = 250)		#
- Ephedrine	88 (35.2 %)	
- Phenylephrine	9 (3.5 %)	
- Norepinephrine	27 (10.8 %)	
- Dopamine	7 (2.8 %)	
- Dobutamine	5 (2 %)	
- Epinephrine	7 (2.8 %)	
Heart Rate		
- Baseline	146.4 ± 19.4	143 ± 19
- Threshold for intervention	98.4 ± 54	81 ± 21
- Number of interventions n (%)	23 (2.5 %)	145 (2.2 %)
Arterial oxygen saturation		
- Baseline %	99 ± 2	98 ± 4
- Threshold for intervention on SpO2 < 90 % n (%)	48 (41.7 %)	40.6 %
- Threshold for intervention on SpO2 < 85 % n (%)	22 (19.1 %)	18.9 %
- Threshold for intervention on SpO2 < 80 % n (%)	45 (39.1 %)	40.5 %
- Number of interventions n (%)	115 (12.4 %)	830 (12.7 %)
Partial pressure in CO2 (mmHg)		
- Baseline PaCO2	47 ± 12.4	43.5 ± 11.2
- Baseline Pet CO2*		
- Number of interventions	49 (5.3 %)	522 (8 %)
- Threshold for intervention high PaCO2*	# #	65 ± 17.2
- Threshold for intervention high PetCO2	45.6 ± 20.9	59.2 ± 15.7
Haemoglobin g/L		
- Baseline	12.2 ± 2.8	12.3 ± 3.0
- Threshold for intervention	8.4 ± 1.4	8.6 ± 1.7
- Number of interventions	43 (4.6 %)	334 (5.1 %)
Near-infrared spectroscopy		
- Baseline %	78.8 ± 11.6	72.3 ± 15
- Threshold for intervention (absolute) %	52 ± 12.8	45.2 ± 13.4
- Threshold for intervention (change) %	29 ± 18.6	30.4 ± 16.7
- Number of interventions	33 (3.5 %)	147 (2.2 %)
Temperature °C		
- Baseline	36.4 ± 0.6	36.5 ± 0.6
- Threshold for intervention for hypothermia	35.3 ± 1.3	34.5 ± 1.5
- Number of interventions for hypothermia	28 (3 %)	293 (4,5%)

* Data are absent or do not allow any statistical analysis. Data are expressed as mean sd or N (%). #: data not available in the original publication of the European cohort. # #: data not available in the French cohort.

Table 4: Outcome at 30 and 90 days of follow up. * Available data for 790 patients. ** Final mortality rate computed on the overall number of patients with a follow-up until post-procedure day 30. Data are expressed as mean sd or N (%). Overall mortality and complication is expressed as percentage with the 95% confidence interval. #: data not available in the original publication of the European cohort.

Factor	French cohort (n = 880)	European Cohort (n = 5609)
Follow up at day 30	790 (89.8 %)	5510 (93.3 %) 4675
Mortality ay day 30	14 (1.6 [95% CI 1 – 3] %)	105 (1.7 [95% CI 1.6 – 1.8] %)
Location at day 30		#
- Home	630 (71.6 %)	
- Hospital	61 (6.9 %)	
- Other hospital	37 (4.2 %)	
- ICU	48 (5.5 %)	
Complications at day 30*	98 (11.1 [95% CI 8.8 – 13.2] %)	850 (15.4 %)
- Neurological	13 (1.5 %)	146 (2.6 %)
- Surgical	40 (4.5 %)	329 (6 %)
- Respiratory	49 (5.6 %)	457 (8.3 %)
- Cardio-vascular	28 (3.2 %)	315 (5.7 %)
- Renal complications	8 (0.9 %)	98 (1.8 %)
- Liver complications	5 (0.6 %)	51 (0.9 %)
Overall mortality at day 30 and 90 **	17 (1.9 %)	136 (2.4 %)