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Procedure volume is one determinant of centre effect in mechanically ventilated patients

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ABSTRACT: Survival rates vary significantly between intensive care units, most notably in patients requiring mechanical ventilation (MV). The present study sought to estimate the effect of hospital MV volume on hospital mortality.

We included 179,197 consecutive patients who received mechanical ventilation in 294 hospitals. Multivariate logistic regression models with random intercepts were used to estimate the effect of annual MV volume in each hospital, adjusting for differences in severity of illness and case mix.

Median annual MV volume was 162 patients (interquartile range 99–282). Hospital mortality in MV patients was 31.4% overall, 40.8% in the lowest annual volume quartile and 28.2% in the highest quartile. After adjustment for severity of illness, age, diagnosis and organ failure, higher MV volume was associated with significantly lower hospital mortality among MV patients (OR 0.9985 per 10 additional patients, 95% CI 0.9978–0.9992; p=0.0001). A significant centre effect on hospital mortality persisted after adjustment for volume effect (p<0.0001).

Our study demonstrated higher hospital MV volume to be independently associated with increased survival among MV patients. Significant differences in outcomes persisted between centres after adjustment for hospital MV volume, supporting a role for other significant determinants of the centre effect.

KEYWORDS: Acute respiratory distress syndrome, databases, factual, intensive care unit, outcome assessment, performance, quality of healthcare

Over the last two decades, advances in the evaluation of healthcare outcomes have shed light on the determinants of survival in patients undergoing various medical and surgical procedures [1–5]. Variations in outcomes are generally believed to stem from differences between institutions, patient characteristics, case mix or organisational factors [3, 4, 6, 7]. Among the factors that lead to differences between institutions (the centre effect), procedure volume, defined as the number of patients receiving a specific procedure in the hospital each year, has been identified as playing a major role [8–12].

Identifying the determinants of the centre effect may suggest means of improving the quality of care [4]. For instance, staffing differences contribute to the centre effect, and the Leapfrog Group has estimated that applying intensive care unit (ICU) physician staffing standards might save >54,000 lives·yr^{-1} [13]. Thus, comparing quantitative performance across institutions may help us to understand how structure and care processes affect patient survival [1, 14, 15].

Acute respiratory failure is common in patients admitted to the ICU [16]. Despite the advances achieved over the last decade, survival has not substantially improved among patients who receive mechanical ventilation (MV) [16, 17]. This fact suggests a need for updating guidelines for MV, and improving the quality and process of care in patients receiving MV. In a large study of 37 acute care hospitals in the USA, the annual volume of patients receiving MV was a major determinant of survival among these patients [11]. However, other studies found no association between volume and outcome, suggesting a need for additional work on larger numbers of patients and hospitals [18–20].

The purpose of this study was to examine the relationship between the number of critically ill

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patients receiving MV (volume) and hospital survival of those patients. The study included 179,197 consecutive patients who received MV over a 2-yr period in the 294 ICUs in the French Ministry of Health (Paris, France) database.

PATIENTS AND METHODS

Source of data

We used the French nationwide database maintained by the Ministry of Health to obtain standardised hospital discharge data on all in-patient stays in public and private hospitals. The standardised forms used to feed the database collect administrative, demographic and medical information on the patients, including dates and type of admission and discharge (and, therefore, length of hospital stay), vital status at hospital discharge, diagnoses classified using the International Classification of Diseases, 10th revision (ICD-10-CM), and procedures classified using the French Medical Procedures Catalogue. The primary diagnosis, either presented at admission or occurring during the hospital stay, is defined as the diagnosis that accounted for the largest part of the care provided during the hospital stay. This information is used to classify the hospital stay using the French equivalent of the diagnosis-related group (DRG) system (*Programme de Médicalisation des Systèmes d'Information*). For patients admitted to ICUs, severity of illness, as measured by the Simplified Acute Physiology Score II (SAPSII), was recorded [21].

Because the Ministry of Health database contains standardised administrative and medical data on all consecutive hospital discharges, it can be used to derive national estimates. However, the order in which diagnoses are made and procedures used are not recorded in the database. To assess the validity of the database information for assessing ICU admissions and diagnoses, we conducted a comparison with data from the medical records of 6,652 patients in five hospitals [22]. Differences in selected in-patient stays occurred for only 0.2% of stays and were chiefly related to patients who were admitted then given MV outside the ICU.

Study populations

The main study population comprised adults ($\geqslant$18 yrs of age) who were discharged from a French public hospital in 2004 or 2005, and who had a SAPSII value $>$0 and a record of receiving conventional MV, indicating that they were very probably admitted to the ICU. Patients who received only continuous positive airway pressure or noninvasive MV were not included. Hospitals that reported $<$100 admissions·yr^{-1}, no deaths over the year and fewer than five MV patients per year were excluded from the analysis. The final dataset consisted of 179,197 patients with MV, in 294 hospitals.

To evaluate the impact of the underlying disease requiring MV, we defined three other study populations, based on ICD-10-CM codes: acute respiratory distress syndrome (ARDS), cardiogenic shock and intoxications (Table S1 in the supplementary material). These are important groups of low- to high-risk medical conditions. Although clinically relevant, patients with sepsis, severe sepsis or septic shock were not considered in this subgroup analysis, as a consequence of the complex coding system for sepsis in the ICD-10-CM (several codes) and the impossibility of adequately distinguishing hospital- from community-acquired sepsis in the chosen database.

Outcome measures

The exposure variable was annual hospital volume, defined as the number of patients who received MV each year in each hospital. Since we studied 294 hospitals over 2 yrs, we had 588 hospital–year units, which were studied separately, since volume in a given hospital may vary from year to year. The main outcome measure was hospital mortality.

Statistical analysis

Statistical analysis was performed by S. Chevret (Biostatistics Depart, Saint-Louis University Hospital and UMRS 717 Inserm, Paris, France).

Descriptive data are presented as median (interquartile range (IQR)). To evaluate the effects of covariates on the binary outcome variable hospital death, we used logistic regression models with random intercepts for each hospital, introducing

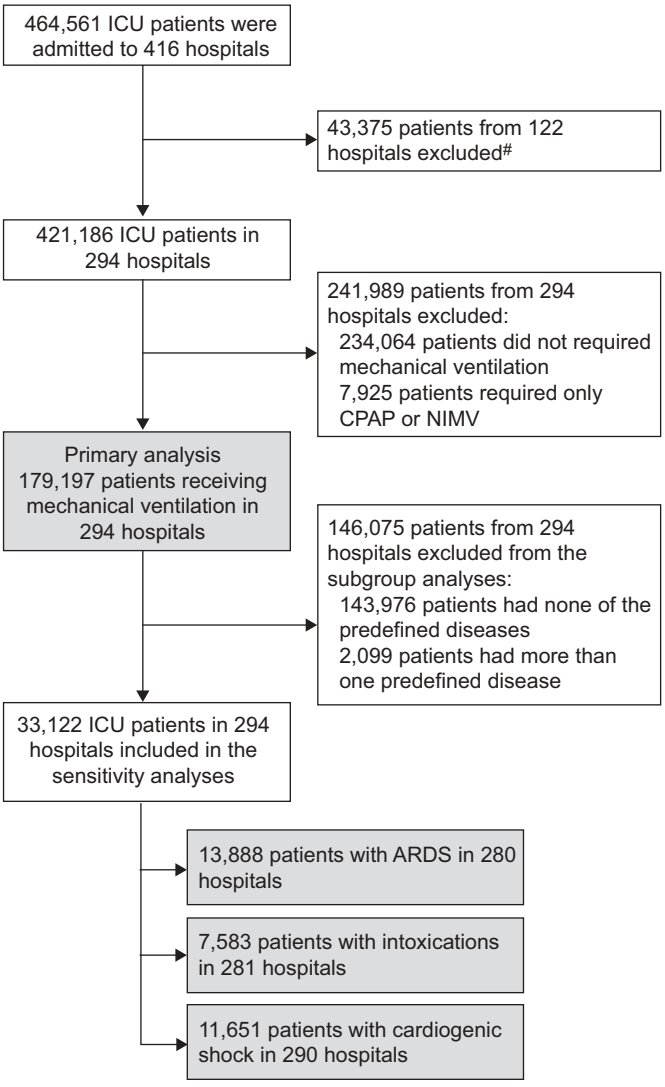

FIGURE 1. Flow chart of patients and hospitals in the study. Shaded boxes represent populations of patients included in the study. ICU: intensive care unit; CPAP: continuous positive airway pressure; NIMV: noninvasive mechanical ventilation; ARDS: acute respiratory distress syndrome. #: reasons for exclusion were $<$100 admissions·yr^{-1} and fewer than five mechanically ventilated patients per year.

hospital volume as a continuous variable. We addressed potential confounding due to case-mix variations by controlling for severity of illness and additional variables related to ICU survival in multivariate models. Severity of illness was assessed based on the SAPSII (with higher scores indicating greater severity of illness and higher risk of death) on the day of admission [21]. To adjust for case mix, secondary analyses were planned in the three study populations (ARDS, cardiogenic shock and intoxications). Given the large sample sizes, only p-values of $\leqslant 0.001$ were considered significant.

Statistical regression models were built using the glmmML function of R to estimate the maximum likelihood *via* numerical integration with the aide of Gauss–Hermite quadrature [23].

RESULTS

In 2004 and 2005, 421,186 patients were admitted to ICUs in the 294 hospitals, and among them, 179,197 patients received MV. Figure 1 shows a flow chart of the patients and hospitals in the study. Median hospital volume was 162 MV patients·year^{-1} (IQR 99–282).

Patient characteristics according to hospital volume

The characteristics of the 179,197 MV patients according to hospital volume are shown in table 1. Median age was 63 yrs (IQR 49–74 yrs) and 111,819 (62.4%) patients were male. Medical DRGs accounted for 57.6% of the hospital stays. In addition to MV, 80,489 (44.9%) patients required vasoactive agents and 16,933 (9.4%) patients required renal replacement therapy. Median length of hospital stay was 14 days (IQR 6–28 days). Median SAPSII at admission was 43 (IQR 29–59), indicating a predicted in-hospital mortality rate of 30.6% (IQR 9.7–66.1%); the observed hospital mortality rate was 31.4%. Reasons for ICU admission and severity of illness evaluated by SAPSII value varied widely with hospital volume. Median SAPSII was lower in high- than in low-volume hospitals (43.7 ± 22.2 in the highest volume quartile *versus* 51.3 ± 22.6 in the lowest volume quartile; $p<0.0001$). This difference in severity of illness probably stemmed, in part, from two other

TABLE 1 Patient characteristics by hospital volume quartile

Characteristics	Hospital volume patients·yr^{-1}			
	<99	99–162	163–282	⩾282
Hospital and ICU characteristics				
Hospitals	146	148	147	147
ICU admissions per yr	68.2±21.4	129.9±19.7	210.7±32.6	809.8±681.3
Patient characteristics				
Patients	9965	19220	30969	119043
Location before ICU				
Home	8836 (88.7)	17054 (88.7)	26665 (86.1)	102653 (86.2)
Age yrs	64.6±17.4	64.0±17.2	61.8±17.5	59.0±17.5
Male %	5753 (57.7)	11440 (59.5)	19004 (61.4)	75995 (63.8)
SAPSII	51.3±22.6	50.5±21.6	51.6±22.2	43.7±22.2
Type of DRG				
Medical	5517 (55.4)	10331 (53.7)	16682 (53.9)	43174 (36.3)
Surgical	2772 (27.8)	5540 (28.8)	8634 (27.9)	59051 (49.6)
Diagnostic category				
ARDS	749 (7.5)	2065 (10.7)	2807 (9.1)	10109 (8.5)
Pneumonia	1900 (19.1)	4699 (24.4)	7320 (23.6)	23389 (19.6)
Severe sepsis/septic shock	1497 (15.0)	3753 (19.5)	6659 (21.5)	18788 (15.8)
Cardiogenic shock	632 (6.3)	1532 (8.0)	2344 (7.6)	8976 (7.5)
Intoxication	592 (5.9)	1198 (6.2)	2037 (6.6)	4302 (3.6)
Status epilepticus	290 (2.9)	577 (3.0)	1091 (3.5)	3374 (2.8)
Status asthmaticus	85 (0.8)	171 (0.9)	312 (1.0)	661 (0.6)
Pancreatitis	120 (1.2)	273 (1.4)	461 (1.5)	1394 (1.2)
Organ failure/life-sustaining therapies				
Vasoactive agents	4073 (40.9)	8864 (46.1)	14910 (48.1)	52642 (44.2)
RRT	376 (3.8)	1548 (8.0)	3192 (10.3)	11817 (9.9)
Coma R402	1805 (18.1)	3667 (19.1)	7507 (24.2)	25801 (21.7)
Acute renal failure N17	1520 (15.2)	3791 (19.7)	6926 (22.4)	22678 (19.0)
Length of hospital stay days	19.2±24.2	22.1±27.2	21.5±27.7	22.4±28.8
Hospital mortality	4062 (40.8)	7347 (38.2)	11356 (36.7)	33607 (28.2)

Data are presented as n, median±SD or n (%). Difference between the four quartiles is statistically significant ($p<0.0001$) for every reported characteristic. ICU: intensive care unit; SAPSII: Simplified Acute Physiology Score II; DRG: diagnosis-related group; ARDS: acute respiratory distress syndrome; RRT: renal replacement therapy.

characteristics of high-volume hospitals, namely, younger patient age (59±17.5 *versus* 64.6±17.4 yrs in the highest and lowest quartiles, respectively; p<0.0001) and larger proportion of patients with surgical DRGs (49.6 *versus* 27.8%; p<0.0001). In high-volume hospitals, there were proportionately more patients requiring vasoactive agents (44.2 *versus* 40.9%; p<0.0001) and/or renal replacement therapy (9.9 *versus* 3.8%; p<0.0001), and patients with coma (21.7 *versus* 18.1%; p<0.0001).

Patients with predefined conditions

Of the 179,197 MV patients, 33,122 (18.5%) patients had one of the three predefined conditions: 13,888 patients had ARDS, 11,651 patients had cardiogenic shock and 7,583 patients had intoxications. The prevalence of these three conditions varied widely between annual volume quartiles (table 1). The condition-specific annual volume (defined as the number of patients with each condition in each study hospital in each study year) was 14 patients·hospital^{-1}·yr^{-1} (IQR 6–30 patients·hospital^{-1}·yr^{-1}) for ARDS, 10 patients·hospital^{-1}·yr^{-1} (IQR 5–20 patients·hospital^{-1}·yr^{-1}) for cardiogenic shock and 10 patients·hospital^{-1}·yr^{-1} (IQR 4–17 patients·hospital^{-1}·yr^{-1}) for intoxications. Hospital mortality was 43.1% in the 33,122 patients overall, 53.7% in patients with ARDS, 59.7% in patients with cardiogenic shock and 2.2% in patients with intoxications.

Impact of hospital volume on outcome

Unadjusted hospital mortality decreased from each volume quartile to the next, from 40.8% in the lowest volume hospitals to 28.2% in the highest (table 1). After adjusting for potential confounders (severity of illness, age, DRG, diagnoses during the ICU stay, organ failures and life-sustaining treatments) and incorporating a random hospital effect, each hospital volume increase of 10 patients·year^{-1} was associated with a significant decrease in hospital mortality (OR 0.9985, 95% CI 0.9978–0.9992; p=0.0001) (table 2). Figures 2 and 3 show the effect of hospital volume on hospital mortality, evaluated as a continuous variable. The multivariate mixed regression model showed persistence of a significant centre effect (p<0.0001).

TABLE 2 Factors associated with hospital mortality: results of the multivariate mixed regression model

Parameter	OR (95% CI)	p-value
Intercept	0.0126 (0.011–0.014)	<0.0001
Hospital volume per 10 patients·yr^{-1}	0.9985 (0.9978–0.9992)	0.0001
Age per yr	1.02 (1.018–1.020)	<0.0001
Female sex	0.90 (0.88–0.93)	<0.0001
SAPS II per point	1.047 (1.046–1.0475)	<0.0001
Surgical DRG	0.46 (0.44–0.47)	<0.0001
ARDS	1.65 (1.58–1.72)	<0.0001
Pneumonia	0.82 (0.80–0.84)	<0.0001
Severe sepsis	1.18 (1.14–1.22)	<0.0001
Cardiogenic shock	1.35 (1.29–1.41)	<0.0001
Intoxication	0.07 (0.06–0.08)	<0.0001
Status epilepticus	0.65 (0.60–0.70)	<0.0001
Status asthmaticus	0.63 (0.54–0.74)	<0.0001
Pancreatitis	0.92 (0.83–1.03)	0.1346
Vasoactive agents	2.41 (2.34–2.48)	<0.0001
RRT	1.79 (1.71–1.87)	<0.0001
Coma	1.71 (1.66–1.77)	<0.0001
Acute renal failure	1.31 (1.26–1.36)	<0.0001

SAPSII: Simplified Acute Physiology Score II; DRG: diagnosis-related group; ARDS: acute respiratory distress syndrome; RRT: renal replacement therapy.

To assess the sensitivity of our findings, we repeated the analysis with varying assumptions about the patient population (table 3). Our results were not affected by the exclusion of outlier hospitals. Nevertheless, total annual hospital volume was no longer associated with hospital mortality when we excluded patients in surgical DRGs (OR 0.9992 per 10 patients·yr^{-1}, 95% CI 0.9984–1.0000; p=0.0502) or when we adjusted for case mix by restricting our analysis to the patients having any of the three predefined conditions (OR 1.0012 per 10 patients·yr^{-1}, 95% CI 0.999–1.002; p=0.06) (table 3).

Impact of hospital volume on outcome of patients with predefined conditions

Although total annual volume (*i.e.* number of MV patients per year in each study hospital) was not associated with adjusted hospital mortality, the condition-specific annual volumes for ARDS and cardiogenic shock (*i.e.* number of patients with each condition per year in each study hospital) was strongly associated with adjusted hospital mortality after adjustment for confounders (table 3). Similarly, the specific hospital random effect correlated positively with the overall hospital random effect in all the populations except the population with intoxications (Figure S2 in the supplementary material).

DISCUSSION

We used data collected over 2 yrs in the French Ministry of Health database to examine the effect of hospital volume on hospital mortality of patients requiring MV. In a population of >170,000 MV patients, hospital volume of MV patients correlated negatively with hospital mortality after adjustment for potential confounders. Interestingly, adjustment for this volume effect did not abolish the centre effect on hospital

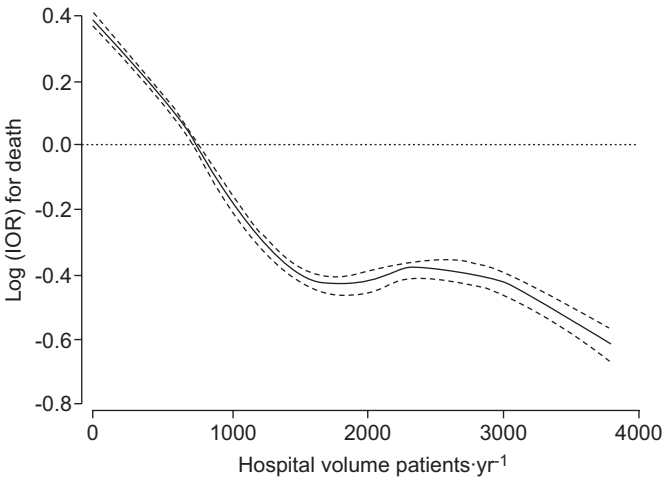

FIGURE 2. Relationship between hospital volume and hospital mortality. —: interval OR (IOR); ---: 95% CI.

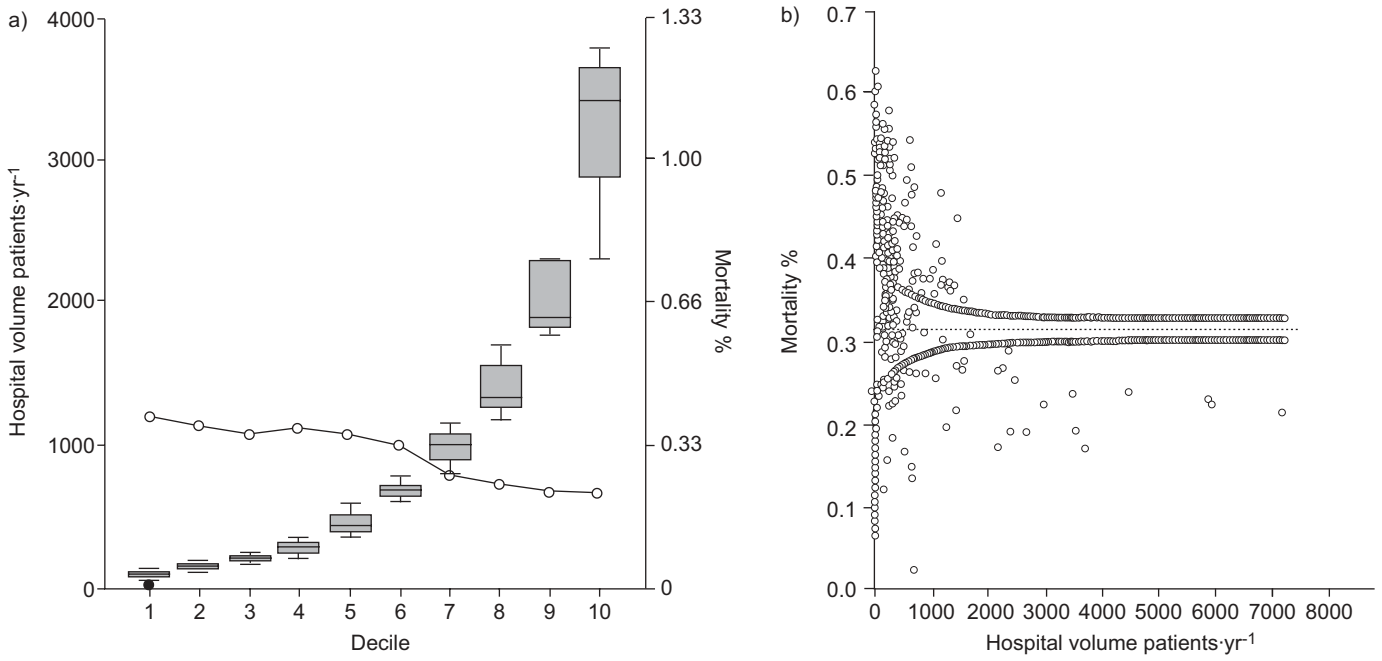

FIGURE 3. Hospital mortality against hospital volume. a) Box plots of annual hospital volumes segregated into ten deciles, with associated hospital mortality (○). Boxes represented the interquartile range and whiskers respresent the 5th and 95th percentiles. —: median; ●: outliers. b) Funnel plot of hospital mortality.

mortality, indicating a role for other factors that remain to be identified.

The association found in our study between higher volume and higher survival, after controlling for confounders, suggests that the greater clinical experience acquired by managing many patients may translate into higher quality of care. Earlier studies found associations between higher volume and better outcomes in several surgical conditions [8, 9, 12]. Conflicting data have been obtained regarding the volume–outcome association in critical care patients, including medical patients, surgical patients, paediatric patients and neonates [2, 10, 11, 20, 24–27]. Several factors may explain these discrepancies. Some of the studies in critically ill patients included small numbers of hospitals [19, 23] and/or patients [20, 24, 28]. Since the effect of hospital volume is usually modest, failure to detect such an effect may indicate inadequate statistical power, especially when adjusting for a cluster effect [29]. In addition, several of these studies were performed in selected ICUs, which may have introduced selection bias [19, 28]. Finally, clustering of the data was disregarded in some studies [19, 28].

Another interesting finding from our study is the impact of condition-specific hospital volumes (*i.e.* annual hospital volume of MV patients with a specific condition), even in the absence of an impact of total hospital MV volume. In sensitivity analyses involving various assumptions about patient populations, after adjustment for confounders, condition-specific hospital volumes were independently associated with hospital mortality. This finding suggests that, even when greater experience with MV has no effect on outcome, greater experience with a specific condition may benefit the patients. Few studies have evaluated the impact of hospital volume of specific diseases. In one study, even an increase of 1 patient·yr^{-1} having a haematological malignancy and acute respiratory failure was associated with a significant decrease in mortality [25]. Similarly, in a study of ICU admissions from 1991 to 1997, high-volume hospitals had lower mortality rates in medical ICU patients with gastrointestinal diseases (hazard ratio 0.68, 95% CI 0.51–0.85) but not in patients with respiratory or neurological reasons for admission [24]. However, each of the groups in this study included a heterogeneous array of conditions, ranging, for instance, from ARDS to chronic obstructive pulmonary disease in the respiratory group, and from metabolic coma to intracerebral haemorrhage in the neurological group. This heterogeneity may explain the absence of associations between volume and mortality [24]. Our results suggest that centres having extensive experience with specific diagnoses may produce the best outcomes. This result suggests that regionalisation of care and patient referral to high-volume centres would be beneficial, at least when dealing with these specific conditions. However, we found no association between hospital volume and mortality in the subgroup of patients with intoxications; the low hospital mortality of 2.2% in this subgroup should be taken into account when interpreting this negative result.

Our study has several limitations. First, the information available on the institutions was limited and we were, therefore, unable to adjust mortality for specific characteristics of the centres. However, the use of a multivariate mixed regression model allowed us to incorporate and test for a random cluster effect of the institutions. Patient referral practices were not evaluated in this study. They may affect the impact of volume on mortality, as well as the performance of healthcare institutions [10, 20, 24]. However, they were probably taken into account as part of the centre effect identified in our study, suggesting that hospital volume is associated with outcome independently of the institutions' characteristics. Another limit arises from the database used.

TABLE 3 Sensitivity analysis for impact of hospital volume on mortality rate

	Patients n	OR (95% CI)	p-value
Base model	179197	0.9985 (0.9978–0.9992)	0.0001
Excluding outlier hospitals#	16279	0.9989 (0.998–0.9998)	0.0226
Excluding patients with surgical conditions	103200		
Effect of total annual volume		0.9992 (0.9984–1.0000)	0.0502
Effect of annual volume of patients with medical condition		0.9999 (0.9997–1.0000)	0.0244
Including only patients with predefined conditions			
All conditions	33122		
Effect of total annual volume		1.0012 (0.9999–1.0025)	0.066
Effect of annual volume for all three conditions		0.9987 (0.9980–0.9994)	0.0003
ARDS	13888		
Effect of total annual volume		1.0005 (0.9994–1.0017)	0.36
Effect of ARDS annual volume		0.9983 (0.9973–0.9993)	0.0010
Cardiogenic shock	11651		
Effect of total annual volume		1.0015 (0.9996–1.0034)	0.1147
Effect of cardiogenic shock annual volume		0.9958 (0.9933–0.9984)	0.0017
Intoxication	7583		
Effect of total annual volume		1.0027 (0.9998–1.0055)	0.0656
Effect of intoxication annual volume		0.9962 (0.9883–1.0042)	0.35

Total annual volume is defined as the total number of patients managed with conventional mechanical ventilation per year. Condition-specific annual volume is defined as the total number of patients with the specific condition managed with mechanical ventilation per year. ARDS: acute respiratory distress syndrome. #: defined as having annual counts below the 5th percentile or above the 95th percentile.

Indeed, we used a database that contains information on all patients discharged from healthcare institutions in France. This database is designed to serve as a tool for cost assessments, as opposed to medical research. Data quality and validity may be problematic in databases that are not specifically designed for research. For example, several pieces of information regarding duration of organ support were lacking. Moreover, misleading coding may have affected DRG for the included patients. Nevertheless, for analysis of hospital volume influence in specific conditions, we choose DRG, for which coding was expected to be robust, as a way to limit this bias. In addition, earlier work showed that administrative databases performed relatively well compared to clinical databases, being capable of identifying outlying hospitals with slight [30] or major [31] differences. Finally, our findings may not apply to other countries. In France, most ICUs have high staffing levels [32] compared to other countries [13, 32]. Nevertheless, our study provides robust information on the impact of hospital volume on hospital mortality in countries with high ICU staffing levels. Our findings support the practice of regionalisation in these countries.

In conclusion, our study, the largest to date in this field, showed that higher hospital volume was associated with lower adjusted hospital mortality among patients requiring MV in a healthcare system characterised by high-level ICU staffing. In addition, condition-specific hospital volumes (*i.e.* annual hospital volume of MV patients having a specific condition) were also associated with hospital mortality in patients with ARDS or cardiogenic shock. Our findings support studies of the regionalisation of care, as well as patient referral to high-volume centres, at least when dealing with these specific conditions. Lastly, the centre effect persisted after adjustment for hospital volume. Therefore, further studies are needed to look for structural or organisational factors associated with this residual centre effect.

SUPPORT STATEMENT

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STATEMENT OF INTEREST

None declared.

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