OUTCOMES AFTER POSTOPERATIVE ICU ADMISSION IN THE ELDERLY IN FRANCE: A POPULATION-BASED COHORT STUDY

By

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A Thesis Submitted to the School of Graduate Studies in Partial Fulfillment of the Requirements for the Degree

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ABSTRACT

Postoperative ICU admission is afforded to patients with high clinical severity, but the benefits and harms of such an endeavour are debateable. The purpose of my thesis was to further understand a) the type of patients being admitted to ICU, b) the role of age in ICU admission, and c) the association (if any) between ICU admission and subsequent mortality and complications.

The thesis consists of 4 chapters. Chapter I provides a brief introduction of the topic and the rationale behind the researched questions. Chapter II examines the association between chronological age and ICU admission in postoperative patients. This analysis sheds light on one of the 17 variables included in the score (*i.e.* age), which drives the clinical severity score in parts of the population. Chapter III uses a propensity score model to match patients that were admitted to ICU and those that were not based on several pretreatment variables, to assess the impact ICU admission has on postoperative mortality and complications. Finally, Chapter IV reflects the conclusions of the thesis and suggests further research agendas.

Overall, these three thesis components will illustrate the role of ICU admission in an adult postoperative population as well as its consequences in comparison to those not admitted to an ICU.

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DECLARATION

The contribution of Pakeezah Saadat to all chapters in the thesis include contributing to research ideas and questions, performing the statistical analyses, interpretation of results, and writing of the thesis. This research was conducted between November 2018 and June 2019.

INTRODUCTION

Background and Rationale

Behind most literature related to Intensive Care Unit (ICU) admission lies one basic question – which type of patient is worth ICU admission directly after surgery? ICUs are resource-intensive and hence, costly. Plenty of studies have tried to answer this question time and again in different populations with varying results. Guidelines pertaining to ICU admission have been drafted mostly on observational studies due to lack of randomised controlled trials, which have not occurred because randomising patients to ICU or other wards irrespective of their medical condition will be unethical.(1) With an ever-growing population requiring more critical care resources, it is important to assess whether the ICU resources are being allocated appropriately. A recent review of ICU resources in Canada showed an increase of 12% from 2007 to 2013 in terms of adult ICU admissions. The daily cost of ICU stay is at least three-times as much as the daily cost of general ward stay.(2) With a rapid increase in ICU admissions and associated high costs, it is pertinent that our systems review admission policies before they become overwhelmed. In fact, all teaching hospital ICUs in Canada operate at 90% capacity with an average of 50 days per year spent overcapacity.(2) The current state of the ICU system will not get better as the complexity of critical illnesses grows in the increasing older population. Therefore, it is important to consider the different factors that impact ICU admission in postoperative patients, their subsequent influence on patient-related outcomes, and whether there is a need to change admission criteria.

Current Issues

Patient's age is often an implicit reason behind a physician's decision to not admit a patient to ICU.(3) However, this decision is often enveloped with comorbidities and other factors that are an indirect consequence of age. There is a tendency among clinicians and systems to use age as an excluding criterion for ICU admission which can be classified as ageism (4). Commentaries on why patients over a certain age should not be afforded certain healthcare interventions have also been published before.(5,6) This idea to deny older patients ICU access is not backed by evidence because two 75-year old patients can have very different life trajectories based on their history. In fact, this bias against the elderly is already found in medicine as Reuben *et al.* showed that medical students are less likely to admit an 85-year-old with acute illness to ICU and treat aggressively than a 10-year-old with chronic leukemia.(4)

In the 1980s, there were calls to cut healthcare budgets pertaining to the elderly to solve issues around constrained ICU resources by reallocating it to a different subpopulation.(6) It is also possible that such behavior could have created an even bigger problem, such as an increase in serious complications and mortalities in those who may have benefitted the most from ICU and rightly deserved it, and above all, it would have been unethical.(6) If we let this potential bias covertly block ICU admissions, we may increase adverse outcomes in patients in which it is easily avoidable. There is no reason why we would not face this issue again in 2019 with an even higher demand for critical resources at all levels of the population. Hence, clinicians and researchers must tackle it responsibly by providing evidence-based insight into how to best manage this potential challenge.

Clinical severity scores are used to assess the risk of complications and mortality in patients based on models developed in specific populations and eras. Our thesis considers SAPS II as it was the only severity score available in the dataset. Simplified Acute Physiology Score (SAPS) II was developed on a European population in 1992. Since then, the characteristics of patients being admitted to ICU may have changed.(7) This is especially concerning as the mean age of patients being admitted to ICU has increased over time which may further demonstrate a link between ICU admissions and mortality (7). Despite calls for the development of a validated prediction tool for admitting the elderly to ICU, no such model has been developed.(8)

In addition, studies assessing postoperative outcomes associated with ICU admissions in various subgroups have relied heavily on prospective and retrospective analyses that may or may not include selection biases and not exportable predictive models. Besides one study by Wunsch *et al.* assessing 3-year mortality after hospital discharge in Medicare beneficiaries, literature on patients matched for admittance or not to ICU is rarely published.(9) This means that confounders are very likely to bias the existing literature.

SAPS II

In our dataset, clinical severity is measured using SAPS II which is currently being used in French ICUs by physicians for the purpose of estimating mortality probability and by health administrations for estimating ICU-associated costs. SAPS II is used to estimate the probability of in-hospital mortality calculated in the first 24 hours after a patient is admitted to ICU. This score ranges from 1 (sick) to 163 (extremely sick) and is based on 17 variables: "12 physiology variables, age, type of admission, and three underlying disease variables".(10) The higher the score, the higher the predicted in-hospital mortality. The population used for the development and validation of this model is mainly European with 28% of the patients coming from the United States and Canada. Burn and cardiac patients were excluded during the development and validation of this model because such patients are often not treated in general ICUs.(10) However, SAPS II is now widely used in cardiac patients.

Scope

Given constrained health resources and the uncertain benefits of postoperative ICU admission, specifically for the elderly, it is important to identify those who are the best fit for such admission. We explored this issue through two research questions:

1. When age is removed from the assessment of clinical severity based on the SAPS II score, how does it impact clinical severity in the younger and older cohort admitted to ICU? In other words, what is the role of age as a determinant of ICU admission? In particular, how is age associated with in-hospital mortality?
2. When matched for age, sex, centers, surgery types, and preoperative comorbidities, how do patients differ with respect to in-hospital mortality and postoperative complications in ICU-admitted vs non-ICU admitted patients? How do these outcomes differ in the elderly (>65 years old)?

We hope to answer these questions via a retrospective analysis of a population-based database from France which documented all available information from January 1st, 2010 to December 31st, 2014.

Significance of the study:

The main intended goal of the thesis was to elucidate the link between age and postoperative ICU admission as well as its association with in-hospital mortality and complications. Hence, this exploratory thesis aimed to inform the perioperative trajectory of surgical patients and to fill a gap in the literature while establishing an evidence base for subsequent research projects exploring similar topics.

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CHAPTER 2: THE ROLE OF AGE IN IN-HOSPITAL MORTALITY AFTER POSTOPERATIVE ICU ADMISSION

Introduction

Admission to an ICU is based on risk stratification which stems from factors, such as age and comorbidities. During the past decades, predictive scores have been developed to estimate the probability of death during or after an ICU admission. Such scores are useful to estimate the severity of the patients admitted to an ICU and some physicians use them to inform the decision to admit or not a patient to an ICU. SAPS II is one such score which estimates the in-hospital mortality of ICU-admitted patients reflecting their clinical severity. While an ICU admission is unlikely to harm, the cost associated with an ICU stay due to specialized human resource and equipment limits bed availability and patients' selection is required. Decisions should ideally be based on the expected benefit of an ICU admission based on risk to patient as predicted by these scores. Therefore, patients not admitted to an ICU are those considered as not severe enough. On the other hand, patients can also be denied an ICU admission due to limited life expectancy (*e.g.* a severely sick patient who is extremely old) for which such intensive treatment is considered futile.

However, such scores have limitations. Predictive scores are often developed for the general population and they may not be optimal for predicting risk in subpopulations like the elderly. Older population often constitute a small percentage of the total population used for the development and validation of many predictive models. Furthermore, these models can get outdated and may no longer be optimal for patients who now have diseases which carried a much higher risk of death in the past (*e.g.*, HIV infection was frequently a major predictor of death in scores developed in the 90s). Instead, these scores can only predict at their best when the population in question mimics the population used for the development of the model.(1) Similarly, patients excluded from the development of the prediction model cannot be optimally assessed using that model. For instance, Le Gall *et al.* excluded burn patients, coronary care patients, and cardiac surgery patients from the SAPS II model.(2) Hence, calculation of the probability of in-hospital mortality for such patients might not be optimal. However, SAPS II has been widely used in cardiac patients in France and is a part of our dataset. This tool is still used in many countries for predicting in-hospital mortality as well as for ICU cost estimations based on average resources as per the severity of the patient.

Age is a predictor of mortality after surgical procedures.(3) While this may be true for physiological age as well as chronological age, recently focus has shifted towards frailty in the elderly population which is related to physiological age.(4) Here, physiological age is dependent on the physiological reserve a person has and represents a critical threshold beyond which the body starts to deteriorate, resulting in dysregulation of functions.(5) While there is no agreed upon definition of frailty,(6) it is often defined as a clinical syndrome caused by the accumulation of functional deficits, such as decreased grip strength, exhaustion, weight loss, slow walking speed, and low physical activity, which may be insignificant individually, but collectively increase one's "burden of chronic disease, vulnerability to adverse events, and diminish physiological reserve".(5) SAPS II, which is more commonly used as a predictor of in-hospital mortality in ICU-admitted patients, does not really account for physiological reserve in patients but takes into account the chronological age and variables reflecting the physiological response of patients. Our aims were to evaluate the impact of age on the probability of being admitted to an ICU and to determine the impact of age on in-hospital mortality among patients admitted to ICU, with a specific focus on the elderly (66 years and older).

Methods

The data was collected from an administrative database (Programme de médicalisation des systèmes d'information: PMSI registry) of all surgical procedures requiring anesthesia conducted between January 1, 2010 to December 31, 2014 in France. This dataset is an exhaustive record of all surgeries performed in France within public and private institutions during the study period. Pediatric patients (age below 18 years old) are managed differently from adult patients; thus, we restricted our study population to adults (≥ 18 years old) and to institutions performing more than 500 procedures per year. This second restriction is supported by the fact that institutions performing 1 or 2 cases/day are not representative of the average perioperative care. We defined ICU as per the administration definition associated to the PMSI registry: a health care unit that can support mechanical ventilation daily.

Objectives

The two main objectives of this chapter were to evaluate the impact of age on ICU admissions by excluding the age variable from SAPS II, and to determine the association between age and postoperative in-hospital mortality in an ICU population.

Statistical Analyses

Descriptive statistics were used to describe cohort characteristics across the entire study population by age groups. These characteristics include age, sex, SAPS II score, modified SAPS II score (SAPS II without age), ICU length of stay, in-hospital mortality, major postoperative complications including myocardial infarction, heart failure, sepsis, renal failure, stroke, and survival after major postoperative complications.

Study dataset was trimmed such that 1st and 99th percentile of SAPS II scores in each age class was removed to minimize outliers.(7) To demonstrate SAPS II model's calibration with our population, we graphed the probability of in-hospital mortality estimated by SAPS II using the following formula against the observed in-hospital mortality. This relationship was provided via a smoothed representation using polynomial curve up to 3rd degree. (2)

$$logit = \beta_0 + \beta_1(SAPS\ II\ score) + \beta_2[\ln(SAPS\ II\ score + 1)]$$

$$logit = -7.7631 + 0.0737\ (SAPS\ II\ score) + 0.9971[\ln(SAPS\ II\ score + 1)]$$

$$\Pr\left(y = \frac{1}{logit}\right) = \frac{e^{logit}}{(1 + e^{logit})}$$

We also graphed the original SAPS II score superimposed on the modified SAPS II score against age across both groups of young (18-65 years) and old (≥ 66 years) using ninth degree polynomial fitting. Modified SAPS II score was calculated by subtracting the points allotted for age variable during the original computation of SAPSII score from each observation.(2) Appendix A1 and A2 enumerate the points allotted for age by category as well as other variables included in the SAPS II score. All statistical analyses were completed using R version 3.16 and Stata version 14.2 (StataCorp LP, College Station, TX, US). Figures were created using OriginPro, Version 90E (OriginLab Corporation, Northampton, MA, US).

Results

Full Population

Among the 35,747,786 patients from 1271 centres who underwent surgery during our study period, 442,665 (1.1%) were admitted to an ICU. Patient disposition is summarized in a flow chart (Figure 4). Main characteristics observed in patients in the full population are summarized in Table 1 and those admitted to an ICU by age groups are summarized in Table 2.

As demonstrated in Table 1, patients admitted to an ICU were female dominated (64%) and were older than the non-ICU group. The medial length of stay was similar in both groups (*i.e.*

3 days). Number of postoperative mortalities and complications differed, with the ICU group demonstrating comparatively higher proportions in both. Similarly, the percentage of survivors with complications was higher in those not admitted (94%) than those admitted to an ICU (68%).

	Not admitted to ICU (n=34,148,736)	Admitted to ICU (n=426,216)
Age, median [IQR]	57 [42, 70]	66 [54, 76]
Female, n (%)	14,556,314 (42.6)	274,995 (64.5)
SAPS II, median [IQR]	--	29 [21, 42]
*Modified SAPS II, median [IQR]	--	18 [11, 31]
°Length of stay, median [IQR]	3 [2, 6]	3 [1, 5]
In-hospital mortality, n (%)	46,863 (0.14)	64,595 (14.6)
¶Major postoperative complications, n (%)	242,947 (0.71)	143,124 (33.5)
Survivors with major postoperative complications, n (%)	229,420 (94.4)	97,565 (68.1)

*Modified SAPS II refers to SAPS II score excluding the age variable. °Excludes patients sent home directly after surgery. ¶ Major postoperative complications refer to myocardial infarction, heart failure, stroke, sepsis, and renal failure.

Table 1: *Baseline characteristics of the full population (N=34,574,952)*

Age and sex distributions in postoperative patients who were admitted to hospital (left panel) and those who were admitted to an ICU (right panel) were not different (Figure 1). Surgeries and admission to hospital related to obstetric was apparent in the distribution with a peak of admission for women in their third decade of age (Figure 1). Females were also more frequently admitted to an ICU than men. It is however unlikely related to only the patients' sex and could be related to the predominance of female sex in the oldest age class observed in France. The deficit of birth related to World War II is clearly observable in both distributions with a dip in the pyramid around 70 years of age, as well as the increase of births which was observed in the late 40s ("Baby Boom") observed around 75 to 80 years of age (Figure 1).

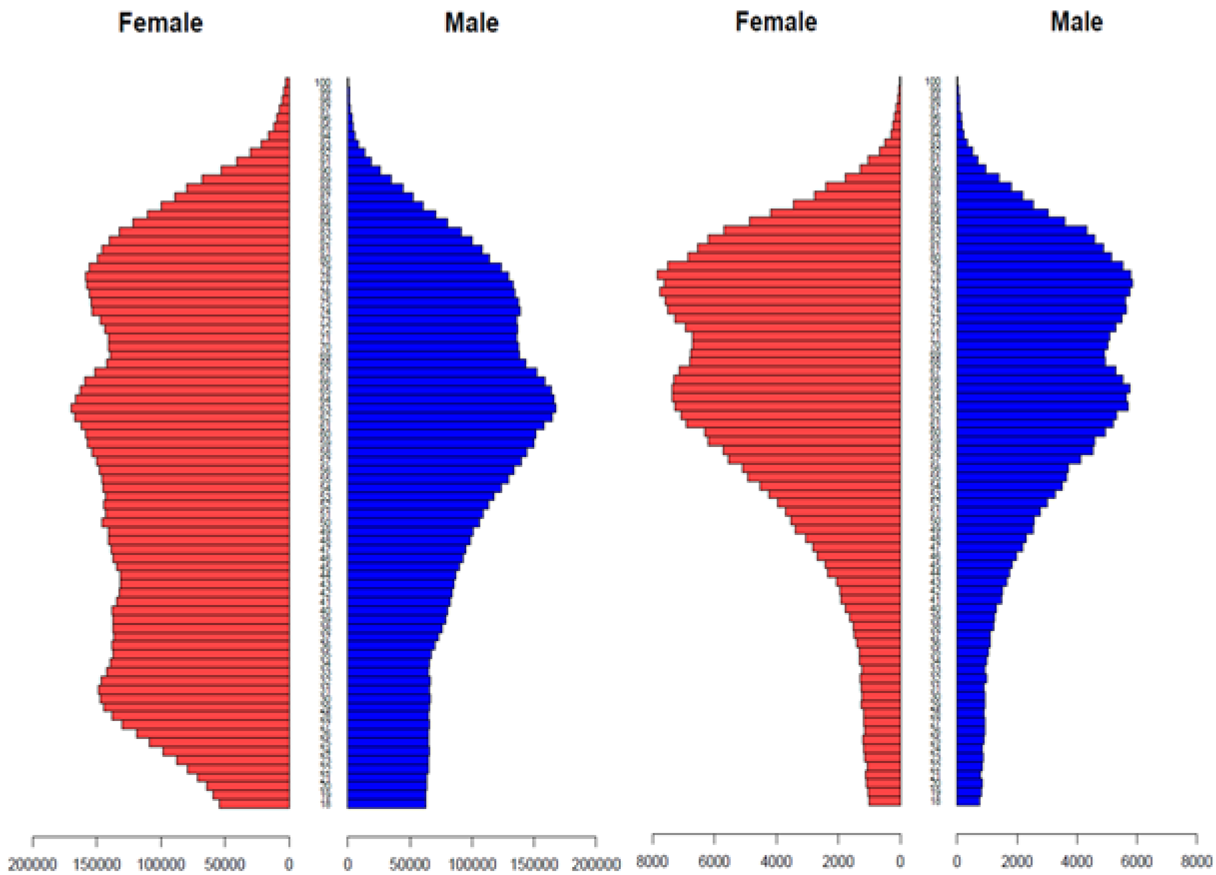

Figure 1: *Age and Sex distribution in patients admitted to hospital (left panel) and those admitted to an ICU (right panel) postoperatively.*

The relationship between age and postoperative outcomes was then estimated (Figure 2). Polynomial fitting up to 9th degree produced a very strong correlation (R^2>0.99) for all relationships (Figure 2). Not surprisingly, the older the patient was the higher was his/her in-hospital mortality after surgery. While the relationship was grossly linear from 18 to 70 years old, we observed a potential inflection point between 70 and 85 years (Figure 2). The second derivative of the fitted relationship between age and mortality was computed (two successive derivations of the fitted 9th degree polynomial function between age and in hospital mortality) and confirmed our observation (Figure 3) showing a sign change in the second derivative (*i.e.* an inflection point) for an age of 78 years. This inflection point, thus, suggests a major change in the relationship between age and mortality at 78 years of age.

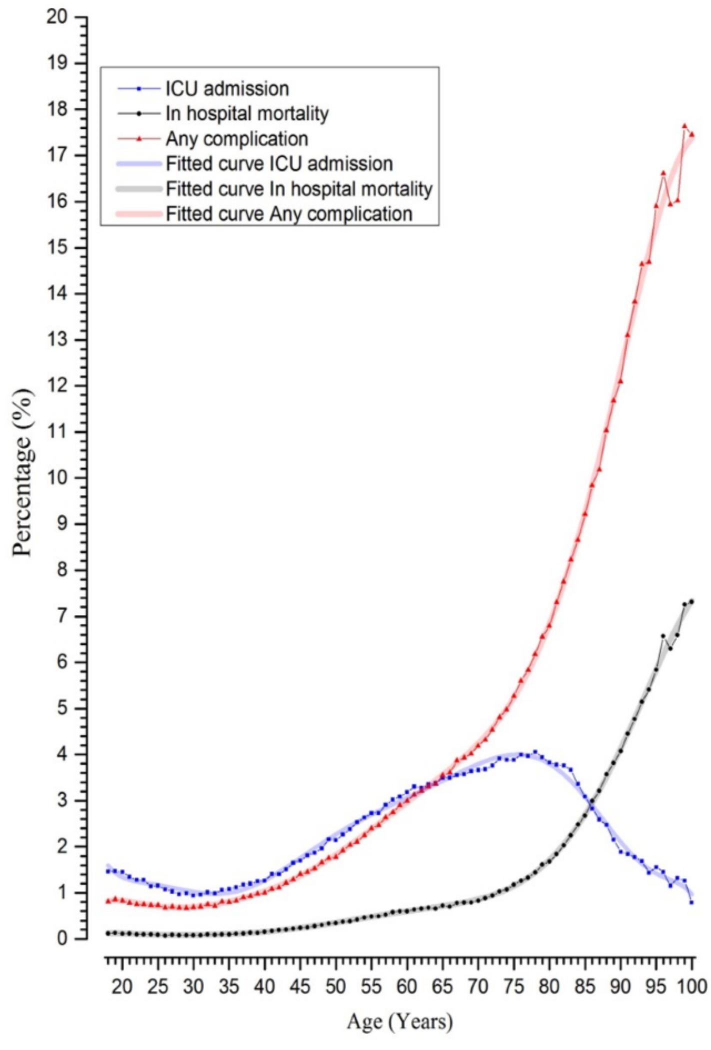

Figure 2: *Percentage of patients by age with ICU admission, in-hospital mortality, and serious complications.*

As depicted in Figure 2, the relationship between age and ICU admission demonstrated a very different shape from mortality and complications. The fitted curves overlap the raw data points depicting an excellent fit. Patients under 30 years old were slightly more frequently admitted to ICU (related to trauma in younger adults). After a pseudo linear increase of ICU admission frequencies, grossly parallel to mortality, we observed a plateau (from 65 to 80 years of age) and then a clear and substantial decrease in the frequency of ICU admission above the age of 85 years. The rate of ICU admission decreased quickly after 80 to 85 years of age to equal the average rate of ICU admission in the entire population (*i.e.* 1%), however the in-hospital mortality in the same categories of age is 8 to 10 times higher than the in-hospital mortality observed in the entire population (Figure 2).

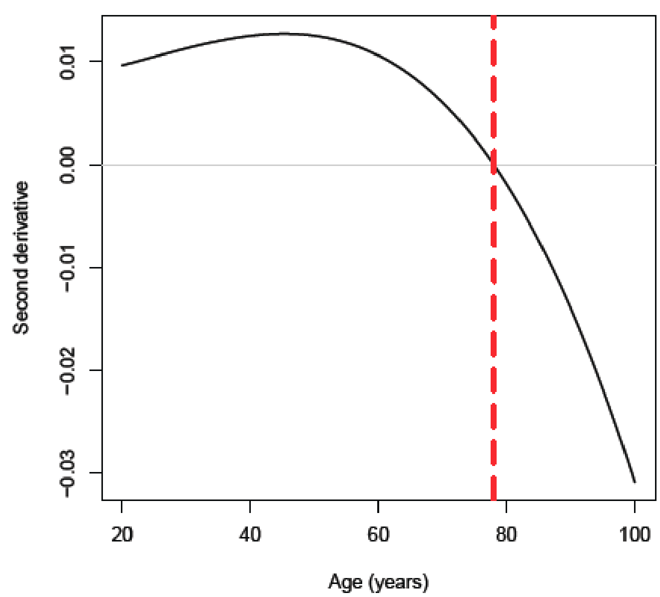

Figure 3: *Second derivative for the mortality fitted curve by age with dashed line highlighting the inflection point.*

ICU population

In order to evaluate the clinical severity of the patients admitted to ICU, we used the SAPS II score which was calculated for every patient admitted to an ICU. Of the 442,665 patients admitted postoperatively to an ICU, 434,832 (98.2%) had a SAPS II score ranging from 1 to 163. Scores that were either missing (0.009%), less than or equal to 0 (1.69%), or greater than 163 (0.064%) were excluded. After trimming, we lost 4.9% of the total population and 404,464 ICU hospitalized patients were included in the analysis (Figure 4).

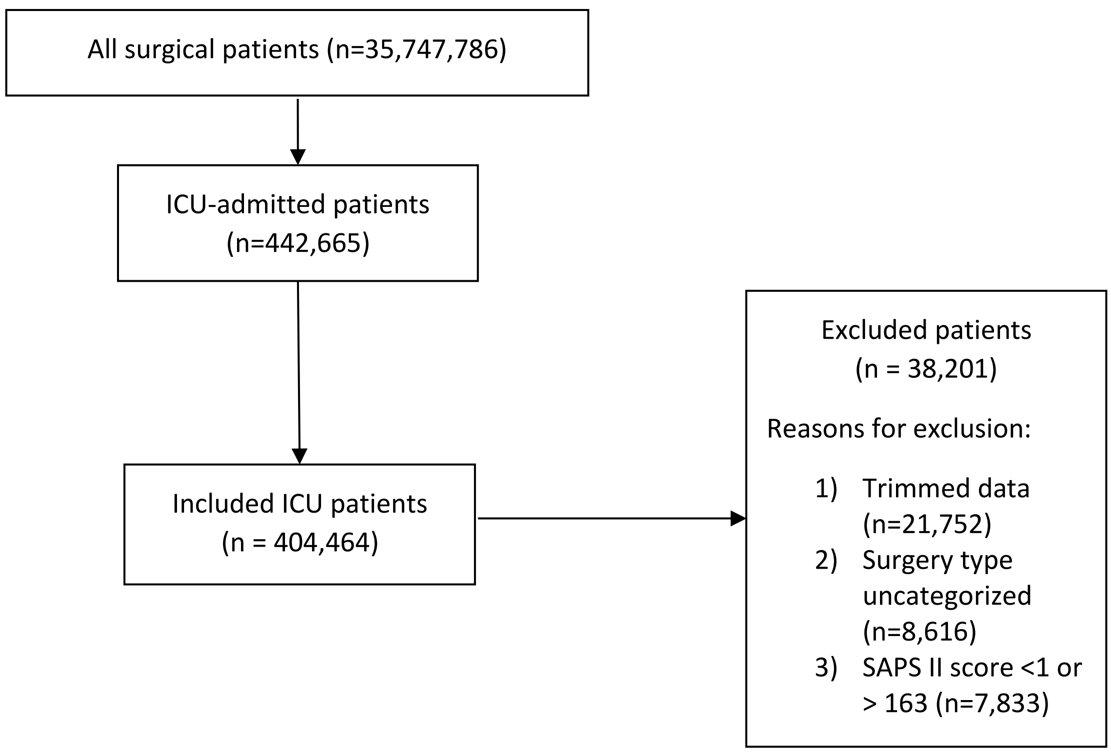

Figure 4. *Flow chart of the included patients*

	Younger patients (18 to 65 years) (N = 190,823)	Older patients (≥66 years) (N = 213,641)
Age, median [IQR]	53 [42, 60]	75 [70, 80]
Female, n (%)	127,038 (66.6)	134,594 (63.0)
SAPS II, median [IQR]	25 [18, 37]	34 [26, 47]
Modified SAPS II, median [IQR]	18 [11, 30]	18 [11, 31]
ICU length of stay, median [IQR]	3 [1, 6]	3 [2, 6]
In-hospital mortality, n (%)	19,594 (10.3)	38,560 (18.0)
Major postoperative complications, n (%)	53,125 (27.8)	84,728 (39.7)
Survivors with major postoperative complications, n (%)	40,060 (75.4)	55,605 (65.6)

Table 2: *Baseline characteristics of the trimmed ICU population (N=404,464)*

As summarized in Table 2, younger patients (≤65 years) had a lower SAPS II score and subsequent in-hospital mortality rate in comparison with the older patients (≥66 years). Of the total mortality, 66.3% of it occurred in older patients. However, the median length of ICU stay did not differ between the two groups (*i.e.* 3 days). In addition, older patients had more major postoperative complications (39.6%) than younger patients (27.8%).

We evaluated the predictive performance of SAPS II in the study population where we used a 3rd degree polynomial fitting to represent predicted mortality and observed mortality against age (Figure 5). Postoperative in-hospital mortality as predicted by SAPS II and observed postoperative in-hospital mortality were well correlated among the range of age (r^2=0.73).

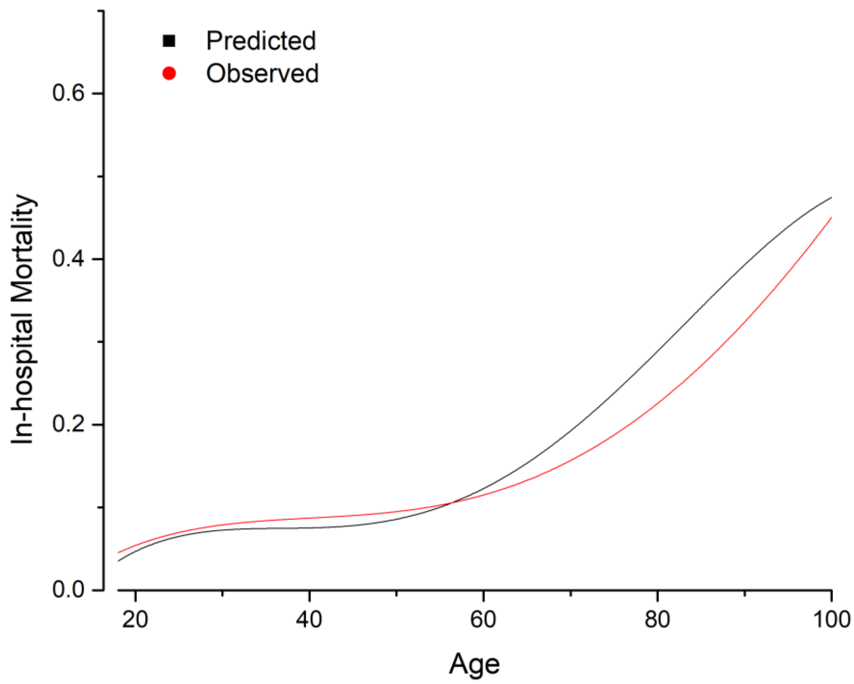

Figure 5: *Predicted vs observed in-hospital mortality in the ICU admitted patients*

Modified SAPS II Score

SAPS II includes age as one of the variables used to estimate the mortality after ICU admission. Knowing the age and the SAPS II value for each patient admitted to an ICU, we calculated for each of these patients a modified SAPS II excluding the age component from the original SAPS II. We did not intend to produce a new predictive score but we aimed to separate the clinical severity summarized by SAPS II from the age of the patient. We used up to 9th degree polynomial fitting to represent SAPS II score and modified SAPS II score against age (Figure 6). The modified SAPS II curve demonstrated an almost-horizontal line up until the age of 75 years, which demonstrates a null relationship between age and clinical severity score. In other words, younger and older patients did not differ on clinical severity based on SAPS II when age < 75 years. The curve rises approximately after 75 years of age, which shows that patients older than 75 had higher clinical severity independent of their age (Figure 6). The clinical severity of patients older than 75 years admitted to an ICU was the highest observed in the entire cohort. This demonstrates that the oldest patients admitted to an ICU have high clinical severity and a poor predicted prognosis upon admission even without considering age.

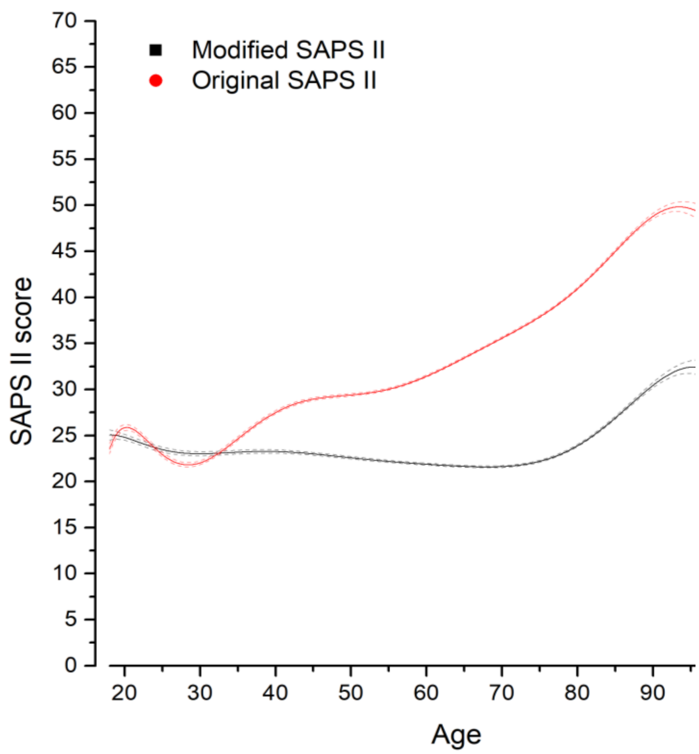

Figure 6: *Original and modified SAPS II scores in the ICU admitted patients with 95% CI*

Redefining old

After examining the graphs, we performed a post-hoc analysis where we redefined "old" as those older than 75 years of age (n = 104,857). This showed that the median modified SAPS II score was 3 points higher in the older cohort than the younger cohort (20 [IQR 12, 33] vs 17 [IQR 11, 29]). Similarly, 22.6% of the older patients had in-hospital mortality as compared to the 11.5%

of the younger cohort. Median length of stay in ICU was the same in both cohorts (*i.e.* 3 days). Additionally, 46,506 patients (44.3%) of the older cohort had major postoperative complications as compared to the 91,347 patients (30.4%) in the younger cohort. In total, 28,544 patients (38.6%) and 67,121 patients (26.5%) with complications in the older and younger cohort died in the hospital, respectively.

Discussion

Our findings demonstrate that with age, there is a sharp rise in postoperative complications and in-hospital mortality, but an opposite trend follows in ICU admissions. We observed a sharp decline in ICU admissions after the age of 75. While in-hospitality mortality increases almost linearly with age among the elderly (≥75 years), they are less likely to be admitted to an ICU despite a markedly worse postoperative outcome. Furthermore, older ICU patients presented a higher modified SAPS II than the younger patients. This denotes that ICU patient selection procedure favors homogenously sick patients among those < 75 years with the sickest patients among the oldest old (≥ 75 years).

In addition, we demonstrated that among patients aged 65 years or younger, clinical severity (as reflected through SAPS II) is not very high and mortality rate is stable as well. In fact, when age is excluded from SAPS II scores, we observe a similar level of severity throughout this cohort, and this suggests that these patients have a comparatively low level of clinical severity irrespective of their age.

We also demonstrated that the younger cohort had a relatively lower number of postoperative complications (27%) and three-fourths of such patients survived ICU hospitalization, in comparison to the older cohort (39%). We hypothesize that this cohort reflects an ideal type of patient who would benefit the most from an ICU admission because of their relatively small number of mortalities (10%) and a high postoperative survival rate.

In terms of the older cohort (≥ 66 years), we observed that patients generally had a higher in-hospital mortality (18%) which may have been due to a higher clinical severity following postoperative complications. When age was subtracted from SAPS II score, patients still had a high score independent of their age. This demonstrated that patients in this cohort died not solely because of their age but also due to clinical severity at ICU admission, as defined by variables other than age (Appendix 1). In comparison, these patients had a higher number of postoperative complications (40%) out of which only 66% survived ICU hospitalization. These patients perhaps did not benefit as much from ICU hospitalization as the younger cohort.

While it is understood that older patients will generally have more postoperative complications than the younger patients given their low physiological reserve, we find that of the 137,853 patients that had major postoperative complications, 69% (n=29,123) of those that died belonged to the older cohort. Once again, we find that the older cohort is at a higher risk for in-hospital mortality due to postoperative complications despite the efforts to preserve life with intensive care.

One might be tempted to conclude that the observed deficit of ICU admission in elderly induced the observed excess of postoperative mortality and that patients' selection for ICU admission based on age is related to the change in the relationship between age and postoperative in-hospital mortality. In other words, one could suggest that a limitation of postoperative ICU admission based on age is responsible for a dramatic increase of mortality in the elderly. Such interpretation may, however, be biased by many potential confounders and our observational approach is not able to clarify the nature of the observed relationship.

Paradoxically, it is possible that older patients may benefit from less intensive care in a general ward, thus reducing the mortality rate while saving valuable resources for those who rightly deserve it. As evidenced by Guidet and colleagues' cluster-randomized trial, doubling the ICU admission rate for older patients yielded no benefit and may have caused harm.(8) This study also established that countries with a higher bed supply should reconsider their ICU admission strategy to maximise any associated benefits and minimize the costs. Our results are similar to a large study by Kahan et al which showed that patients admitted to critical care directly after surgery had higher odds of mortality (OR 3.01; 95% CI 2.10 to 5.21) with slightly higher odds ratio for patients from low and middle income countries.(9) As elucidated before, one reason for higher mortality rates especially in the older population is a low physiological reserve which is best reflected by frailty. This was supported by Flaatten *et al*. in their prospective cohort study where they showed that increasing class of frailty at the time of ICU admission was associated with higher risk of mortality (Hazard Ratio 1.54; 95% CI 1.38 to 1.73).(10) This study reinforces the idea that frailty could be used as a pre-admission tool to assess patient's survival probability and functional outcome in an ICU. Despite the clinical sense of this approach, we must recognize that we still have no consensual or pragmatic definition of "frailty" in 2019.

Our study presented some limitations. While unplanned surgical procedures lead to poorer outcomes, this information was not available in our dataset and we were not able to appropriately adjust our analyses for it.(11) Second, our findings cannot be linked to a specific long- or short-term (for instance, 30-day mortality) outcome since there was no standardized follow-up. Third, mortality after ICU-discharge was not available due to the law restrictions associated to the use of the French national mortality database (crossing major datasets requires specific authorization, very unlikely to be obtained in our case). Lastly, the objective of this chapter was to compare ICU admissions among the younger and older French patients which limited our ability to provide a conclusion in comparison with those not admitted to ICU.

The strength of our study is that we considered the full population of eligible adult patients, men and women, admitted to ICU postoperatively over a period of 5 years in France. France has a healthcare system and a population, in terms of age distribution, that is similar to Canada's which likely makes the results of this study generalizable to this population as well. We included all ICU admissions without any restrictions to length of stay or admission type; hence the results should have an acceptable external validity.

Conclusion

Postoperative mortality in patients older than 75 was 8 to 10 times more frequent than the average mortality observed in the entire cohort. However, postoperative ICU admission in patients older than 75 was lower than the average ICU admission rate observed in the entire population. While we were not able to confirm the mechanism involved, we detected a significant change in the relationship between age and postoperative mortality in patients older than 75. Furthermore, the clinical severity at admission without considering age (modified SAPS II) was higher in these patients, suggesting that ICU admission in elderly was less frequent and more focused on sickest patients when considered in light of younger patients. We hypothesize that a different ICU admission protocol in elderly could select less severe patients with a better chance to benefit from ICU care.

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CHAPTER 3: POSTOPERATIVE OUTCOMES IN ICU PATIENTS COMPARED WITH NON-ICU PATIENTS

Introduction

The Global Commission on Surgery's 2030 goal aims at increasing access to surgical procedures to those in need. Currently, 5 billion people lack access to safe and affordable surgical and anesthesia care with another 143 million requiring additional procedures annually to save lives, primarily in low- and middle-income countries.(1) Recent estimates show that about 310 million people undergo surgical procedures each year globally with more than half of all ICU population being patients older than 65 years in the US.(1) Another reason for increasing surgical procedures, especially in the Western countries, is an increased life-expectancy with people living up to the age of 80 to 90 years seeking surgical procedures. The Commission's 2030 target aims to provide 5000 procedures per 100,000 population which will indirectly lead to an increased demand of critical care in a system already troubled with constrained resources.(1)

Studies have shown an incidence of up to 43% postoperative complications and up to 5% postoperative mortality which can likely increase with an increased use of critical care resources.(3) Admission to intensive care unit (ICU) is considered to be a means of mitigating postoperative risks in patients; however, there is little evidence on how such resources should be allotted for different sub-populations to decrease risks and improve health quality. In fact, critical care admission to certain segments of the population like the elderly is a hotly contested argument with a recent UK study reporting that the elderly patients are denied surgical procedures, often based on age alone.(4) Some physicians believe that elderly patients do not benefit from ICU admission at all.(5)

With such inconsistent evidence, it is important that we understand who is likely to benefit from ICU resources and who is unlikely to benefit, *i.e.* increase in morbidity or mortality risk. Our primary objectives were to determine the impact of postoperative ICU admission on in-hospital mortality and postoperative complications in adults, with a specific focus on the elderly (65 years and older).

Methods

Study Design and Participants

We conducted a population-based propensity-score matched cohort study of individuals undergoing surgical procedures to examine in-hospital mortality and postoperative complications. The data was collected from an administrative database Programme de médicalisation des systèmes d'information (PMSI) registry of the adult population in France involving all surgical procedures requiring anesthesia conducted between January 1st, 2010 to December 31st, 2014. Dataset was restricted to hospitals and clinics performing more than 500 procedures per year resulting in the inclusion of 1271 centers with 35,747,786 patients.

For each patient admitted to the ICU, we used propensity-based matching to identify one control who was not admitted to ICU. Admission after the surgical procedure to non-ICU consist of surgical patients admitted to general ward, surgical ward, stepdown units, or sent home. For ease, we will refer to this group as those not admitted to an ICU. Second, each ICU admitted patient was matched to a non-ICU patient based on its closeness in propensity score.

Variables

While the study extracted many variables from the database, only a selected few were considered for the analyses. For each patient, we extracted their age, sex, comorbidities (coded according to the *International Statistical Classification of Diseases and Related Health Problems,* *10th Revision* [ICD-10]), IGS-II (*Indice de Gravite Simplifie II*) score (also known as SAPS II (Simplified Acute Physiology Score) in English) for ICU-admitted patients, center code where procedure was performed, procedures performed during hospital stay (coded according to the French classification for medical procedures in the Classification Commune des Actes Medicaux [CCAM]), length of stay in hospital, ICU, standard ward, and stepdown unit, postoperative in-hospital complications and mortality.

All postoperative medical conditions are acute, but their exact timing is unknown (*i.e.* before ICU admission, during ICU admission, or after ICU admission). Therefore, it is assumed that they occurred either during or after ICU admission.

Outcomes of Interest

The primary outcome was in-hospital mortality, defined as death after surgery and prior to hospital discharge, regardless of length of stay. We also studied several postoperative secondary outcomes that were prespecified including myocardial infarction, heart failure, stroke, renal failure, and sepsis.

Assembly of study cohort: propensity score matching

Propensity scores are mainly used when the available data is non-randomized or observational in nature. It is used to assign the probability of being placed in treatment (*e.g.* ICU admission) or control group (*e.g.* standard ward admission) to each of the study participants based on their pre-treatment observed covariates.(6–8) We used multivariable logistic model followed by a propensity score matching algorithm with a 1:1 matching ratio and a caliper of 0.2 Standard Deviation (SD) (≈0.0105) of mean propensity score with no replacement to match ICU admitted patients to those not admitted to ICU after the surgical procedure. The logistic model used to determine the propensity score included the following pretreatment variables: age, sex, center, type of surgery, atrial fibrillation, anemia, cardiac arrhythmia, cancer, chronic obstructive pulmonary disorder (COPD), chronic respiratory failure, cardiovascular disease, dementia, depression, diabetes, dialysis, hypertension, ischemic heart disease, liver disease, metastatic solid tumor, obesity, chronic alcohol abuse, peripheral vascular disease, renal disease, and valvular disease (Table 2). Predictors with less than 0.10% of the observed outcome in the entire study cohort were not included in the model (Table 3). Patients not on common support or unmatched were discarded from the intervention effect analysis.

Assessment of covariate balance

To check imbalance in covariates after matching, standardised difference *d* was calculated for each covariate followed by c-statistic. The c-statistic, ranging from 0.5 to 1, provides information on propensity model's discrimination between the newly created groups *i.e.* treated (ICU) and control (non-ICU), where a high c-statistic represents better discrimination. Standardised difference of greater than 10% was considered as imbalance. Imbalanced variables were adjusted for in the logistic regression model evaluating the association between ICU admission and outcomes in the matched population (double robust approach).

Above mentioned propensity score modeling approach was replicated in an exclusively older population (>64 years) as well.

Statistical Analyses

To compare cohort characteristics, baseline covariates were described using descriptive statistics. Under non-Normal Distribution, continuous data were described as median and interquartile range, and dichotomous data were always described as numbers and percentages. We did not perform any statistical testing to extract *p* values because with such a large sample size, significant differences occur often. We evaluated the association between ICU admission status and subsequent complications and in-hospital mortality. We graphed the density of propensity score by treatment variable (*i.e.* ICU admission) showing common support. We also created population pyramid for the matched cohort. Associations between treatment and outcomes are presented using relative risks (RR) with 95% confidence intervals (CI) as well as adjusted odds ratios (OR) with 95% CI for uncommon outcomes (incidence rate < 10%). In addition, we report types of surgical procedures with the total number of in-hospital mortalities, ICU admission, deaths in ICU, and unadjusted incidence estimate per surgery type.

Statistical analyses were performed using Stata 14.2 software (StataCorp LP, College Station, TX, US) and some figures were created using OriginPro, Version 90E (OriginLab Corporation, Northampton, MA, US).

Results

We identified 35,747,786 eligible patients during the study period from 1271 centers in France that were included in the study. Of these, 442,665 patients were admitted to the ICU postoperatively whereas 35,304,923 patients were not admitted to ICU. In total, 1,172,834 (3.3%) patients were dropped with a total of 34,547,952 included in the analysis. Figure 1 is a flowchart of how observations were counted as eligible and lists the reasons for excluding observations. Table 1 reports the baseline patient characteristics of the two groups.

Unmatched population

In the unmatched study population, there were more patients not admitted to ICU (98.7%) than ICU (1.3%). Women formed a majority for ICU admission (64.5%). ICU and non-ICU patients had a median age of 66 years (IQR 54 to 76) and 57 years (IQR 42 to 70), respectively. Patients admitted in ICU were from 323 distinct geographical centers whereas patients not admitted to ICU were from 1256 distinct centers. The median length of stay in ICU and other units was 3 and 8 days, respectively. Patients' characteristics are summarized in Table 1.

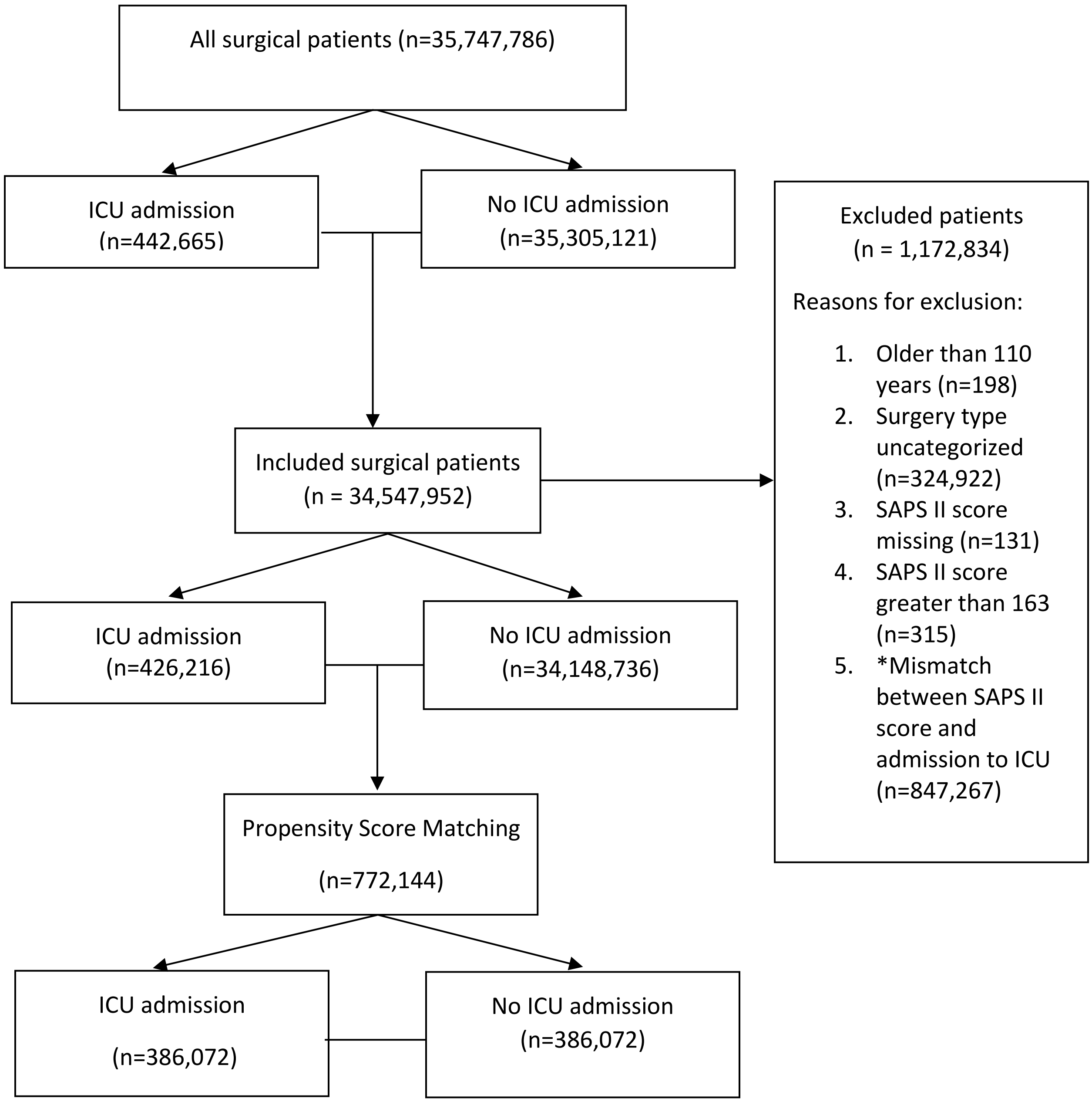

Figure 1: *Flow chart of matched cohorts*

*Patients with no SAPS II score but with indication of ICU admission were dropped. Similarly, patients with a SAPS II score but no indication of ICU admission were dropped.

Matched Population

- *Patient characteristics*

In the matched study population, 386,072 patients were admitted to the ICU postoperatively and another 386,072 patients were not admitted to ICU. Approximately, 65% of the cohort were women in both groups. ICU-admitted patients were 4 years younger than other patients (median: 65 vs 69 years). Similarly, they had the surgical procedure done from 323 distinct centers as compared to the 1158 centers in the other cohort. The average SAPS II score in the matched cohort was similar to that in the unmatched population (34.08 vs 34.05). Finally, the ICU admitted patients had a length of stay one day shorter than the non-ICU patients (3 vs 4 days).

After matching, a few variables had standardised differences greater than 10% including age, surgery type, cancer, grafted transplanted organ, hypertension, and pulmonary circulation disorder, which were adjusted for in the logistic regression model. Since all outcomes were rare (incidence rate <10%), odds ratio was used to describe outcomes. The global imbalance before double robust analysis was summarized by a c-statistic of 0.873, whereas the matching c-statistic was 0.609. Table 2 and Table 3 summarized the variables included or not in the propensity score matching model. Figure 2 shows the overlap of propensity scores in the matched cohorts and Figure 3 shows the comparison of age distribution in patients belonging to the two study groups after matching.

	Unmatched population (n = 34,574,952)			Matched Population (n=772,144)		
Demographics	***Admitted to ICU (n= 426,216)***	***Not admitted to ICU (n= 34,148,736)***	****ASD %***	***Admitted to ICU (n=386 072)***	***Not admitted to ICU (n=386 072)***	****ASD %***
Age, median (IQR)	66 [54 – 76]	57 [42 – 70]	42.08	65 [54, 76]	69 [57, 79]	17.69
Women (%)	274,995 (64.5)	14,556,314 (42.6)	44.99	248,397 (64.3)	253,452 (65.6)	2.74
Distinct centers	323	1256	3.70	323	1158	0.37
¶Distinct surgery types	18	18	78.91	18	18	22.93
Medical History, n (%)						
Atrial fibrillation	96,470 (22.6)	497,221 (1.5)	68.80	78,909 (20.4)	77,966 (20.2)	0.60
Anemia	17,317 (4.1)	219,049 (0.6)	22.72	14,163 (3.7)	15,143 (3.9)	1.32
Cardiac arrythmia	66,782 (15.7)	592,172 (1.7)	51.02	56,769 (14.1)	60,775 (15.7)	2.88
Cancer	87,767 (20.6)	2,769,121 (8.1)	36.18	83,775 (21.7)	106,156 (27.5)	13.49
Chronic heart failure	9,994 (2.3)	51,824 (0.1)	19.84	8,407 (2.2)	7,720 (2.0)	1.24
COPD	31,300 (7.3)	244,975 (0.7)	34.18	26,932 (6.9)	30,595 (7.9)	3.61
Chronic respiratory failure	16,106 (3.8)	59,080 (0.2)	26.12	13,226 (3.4)	14,051 (3.6)	1.15
Cardiovascular disease	8,465 (2)	72,667 (0.2)	17.06	7,525 (1.9)	9,366 (2.4)	3.26
Dementia	5,110 (1.2)	157,307 (0.5)	8.14	4,855 (1.3)	7,870 (2.0)	6.13
Depression	12,695 (3)	327,426 (1)	14.57	11,777 (3.0)	16,598 (4.3)	6.64
Diabetes	76,622 (18)	1,363,471 (4)	45.88	68,619 (17.8)	81,717 (21.2)	8.57
Dialysis	10,944 (2.6)	89,392 (0.3)	19.61	9,945 (2.6)	12,295 (3.2)	3.64
Drug abuse	2,723 (0.6)	29,334 (0.1)	9.21	2,493 (0.6)	1,031 (0.3)	5.62
Grafted transplanted organ	7,224 (1.7)	27,300 (1.7)	17.28	6,976 (1.8)	1,907 (0.5)	12.33
Hemiplegia or paraplegia	6,792 (1.6)	49,227 (0.1)	15.66	6,104 (1.6)	2,259 (0.6)	9.63
Hypertension	176,554 (41.4)	3,892,512 (11.4)	72.43	157,353 (40.8)	177,231 (45.9)	10.40
Pulmonary circulation disorder	13,304 (3.12)	10,739 (0.03)	25.00	10,728 (2.78)	3,273 (0.85)	14.51
Ischemic heart disorder	119,600 (28.1)	502,735 (1.5)	80.83	100,791 (26.1)	105,939 (27.4)	3.01
Liver disease	14,520 (3.4)	158,677 (0.5)	21.47	13,126 (3.4)	15,885 (4.1)	3.75
Metastatic solid tumor	23,784 (5.5)	264,032 (0.8)	27.67	23,062 (6)	31,247 (8.1)	8.29
Obesity	57,145 (13.4)	1,303,585 (3.8)	34.69	49,744 (12.9)	56,968 (14.8)	5.42
Chronic alcohol abuse	24,839 (5.8)	177,176 (0.5)	30.64	22,374 (5.8)	27,858 (7.2)	5.76
Psychoses	3,303 (0.8)	24,596 (0.07)	10.84	2,970 (0.8)	799 (0.2)	8.07
Peripheral vascular disease	65,571 (15.4)	292,189 (0.9)	55.17	55,416 (14.3)	63,161 (16.4)	5.56
Renal disease	31,079 (7.3)	230,516 (0.7)	34.32	26,979 (7)	31,410 (8.1)	4.34
Valvular disease	108,299 (25.4)	186,723 (0.5)	79.63	85,218 (22.1)	72,285 (18.7)	8.32
SAPS II score, mean±SD	34.05±19.02	--	--	34.08 ±19.19	--	--

Table 1. *Baseline characteristics in the unmatched and matched study populations for ICU vs non-ICU patients*

*****Absolute Standardized Difference. ¶ Eighteen main surgery types were included in the analysis.

Predictors	Percentage of the outcome
Atrial fibrillation	1.72
Anemia	0.68
Cardiac arrythmia	1.91
Cancer	8.26
Chronic obstructive pulmonary disorder	0.80
Chronic respiratory failure	0.22
Cardiovascular disease	0.23
Dementia	0.47
Depression	0.98
Diabetes	4.17
Dialysis	0.29
Hypertension	11.77
Ischemic heart disease	1.80
Liver disease	0.50
Metastatic solid tumor	0.83
Obesity	3.94
Chronic alcohol abuse	0.58
Peripheral vascular disease	1.03
Renal disease	0.76
Valvular disease	0.85

Table 2. *Predictors included in the propensity score matching model*

Predictors	Percentage of the outcome
Chronic heart failure	0.18
Drug abuse	0.10
Grafted transplanted organ	0.10
Hemi- or paraplegia	0.16
Pulmonary circulation disorder	0.07
Psychosis	0.08

Table 3. *Predictors excluded from the propensity score matching model*

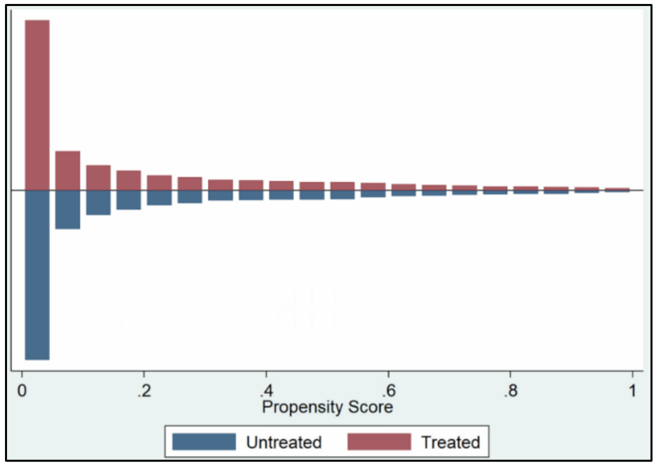

Figure 2. *Propensity scores in the ICU (treated) vs non-ICU (untreated) study groups after matching*

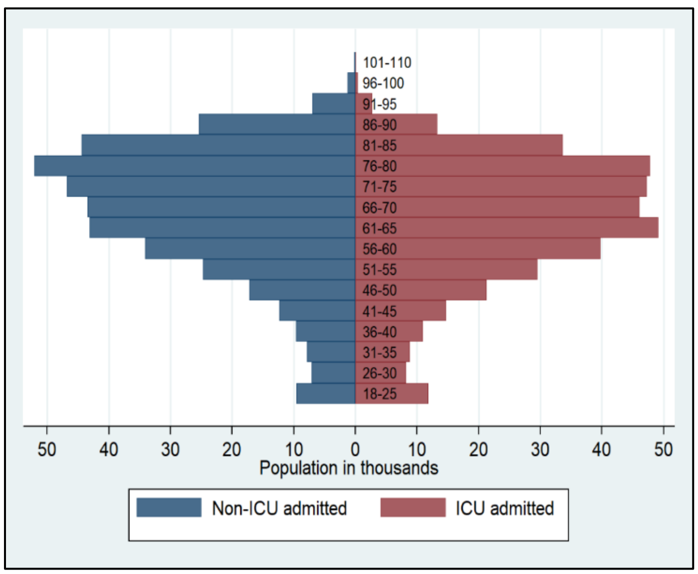

Figure 3. *Comparison of age distribution in patients admitted to ICU or not admitted to ICU after matching*

Association between ICU admission and in-hospital mortality and postoperative complications

Table 4 reports primary and secondary outcomes for the matched cohort. In the matched cohort, 57,675 (14.9%) ICU admitted patients as compared to the 5,922 (1.5%) patients not admitted to ICU died in the hospital. The odds were 13.8 times higher that an ICU admitted patient died in hospital compared to one not admitted to ICU (95% CI 13.4 to 14.2). Overall, non-survivors had a higher severity of disease as illustrated by the higher SAPS II score (mean 60.46±22.01 vs 29.51±14.14). The median length of stay of ICU admitted patients was 3 days, same as the unmatched population.

	ICU patients (n)	Non-ICU patients (n)	Adjusted Odds Ratio, 95% CI	RR, 95% CI
Mortality	57,675 (14.94)	5,922 (1.53)	13.792 (13.417, 14.178)	11.530 (11.270, 11.794)
MI	12,727 (3.30)	2,476 (0.64)	4.580 (4.381, 4.788)	4.477 (4.288, 4.674)
Heart Failure	45,263 (11.72)	19,654 (5.09)	2.298 (2.257, 2.341)	2.156 (2.121, 2.191)
Stroke	14,224 (3.68)	2,159 (0.56)	7.106 (6.787, 7.439)	6.871 (6.574, 7.180)
Renal Failure	54,233 (14.05)	4,568 (1.18)	14.949 (14.496, 15.418)	12.831 (12.499, 13.171)
Sepsis	49,216 (12.75)	4,114 (1.07)	15.739 (15.237, 16.258)	13.603 (13.230, 13.984)

Table 4. *Postoperative outcomes in the full population*

Sepsis was more common in patients admitted to ICU than all other postoperative complications (OR 15.73; 95% CI 15.23 to 16.25) with heart failure being the least common outcome among such patients (OR 2.29; 95% CI 2.25 to 2.34). Overall, 144,063 (37.32%) patients in the ICU cohort had postoperative complications whereas only 33,690 (8.73%) patients had postoperative complications in the other group. Of the patients with at least one complication, 57,675 (40.03%) had in-hospital mortality in ICU whereas 5,922 (17.57%) patients not admitted to ICU also faced in-hospital mortality.

Type of Surgery and Postoperative In-hospital Mortality

Postoperative mortality was observed in 63,597 patients who represented 8.23% of the matched study cohort. Overall, there were significant variations in terms of in-hospital mortality by surgical procedures with cardiac surgery representing the lowest in-hospital mortality (OR 1.35; 95% CI 1.25 to 1.46) and endoscopy representing the highest in-hospital mortality in ICU admitted patients (OR 2272; 95% CI 1055 to 5780). In patients undergoing orthopaedic surgery – the most common surgical procedure amongst non-ICU patients – the odds of in-hospital mortality were 11.7 times higher in ICU admitted patients than in those not admitted to ICU (95% CI 10.86 to 12.58). Table 5 reports unadjusted incidence of in-hospital mortality in the matched study cohort according to the surgical procedure.

	Total Procedures (n, %)	Total Deaths (n, %)	ICU admission (n, %)	Deaths in ICU (n, %) *	Unadjusted estimate, Incidence
Digestive Surgery	105,903 (13.7)	16,751 (26.3)	58,258 (15.0)	15,683 (27.1)	15.81
Cardiac Surgery	160,317 (20.7)	10,471 (16.4)	146,183 (37.8)	9,761 (16.9)	6.53
Neurosurgery	64,481 (8.3)	8,378 (13.1)	38,861 (10.0)	8,187 (14.1)	12.99
Vascular Surgery	72,434 (9.3)	7,807 (12.2)	26,557 (6.8)	6,502 (11.2)	10.77
Orthopaedic Surgery	74,297 (9.6)	4,728 (7.4)	21,238 (5.5)	3,767 (6.5)	6.36
Thoracic Surgery	28,752 (3.7)	3,353 (5.2)	20,243 (5.2)	3,149 (5.4)	11.66
Liver, Biliary Tract	26,297 (3.4)	3,251 (5.1)	15,081 (3.9)	3,103 (5.3)	12.36
Urologic Surgery	59,587 (7.7)	2,492 (3.9)	13,778 (3.5)	1,927 (3.3)	4.18
Plastic Surgery	28,912 (3.7)	1,411 (2.2)	6,692 (1.7)	1,171 (2.0)	4.88
Multiple Trauma	8,972 (1.1)	1,297 (2.0)	8,440 (2.1)	1,272 (2.2)	14.45
Transplant Surgery	7,637 (0.98)	915 (1.4)	7,012 (1.8)	910 (1.5)	11.98
Any Type	12,623 (1.6)	743 (1.1)	5,834 (1.5)	731 (1.2)	5.88
Cardiorhythmology	46,435 (6.0)	715 (1.1)	4,241 (1.0)	408 (0.70)	1.53
ENT Surgery	16,394 (2.1)	633 (0.99)	7,126 (1.8)	540 (0.93)	3.86
Gynaecologic Surgery	18,928 (2.4)	390 (0.61)	3,966 (1.0)	320 (0.55)	2.06
Endoscopy	15,934 (2.0)	192 (0.30)	366 (0.095)	185 (0.32)	1.20
Ophthalmology	20,883 (2.7)	48 (0.075)	395 (0.10)	37 (0.064)	0.22
Caesarean Section	3,358 (0.43)	22 (0.034)	1,801 (0.46)	22 (0.038)	0.65

*****Deaths in ICU represents patients who died a) in ICU or b) after discharge from ICU.

Table 5. *Postoperative in-hospital mortality after main surgical procedures in the matched cohort*

Older population:

As observed in Chapter 2, older patients had lower ICU admission rates followed by higher mortality rates, which demonstrated that sicker patients are more likely to be admitted to ICU. Hence, we replicated the propensity score matching analysis in the older population (>64 years) to understand the difference between ICU and non-ICU admitted patients in this older population.

Unmatched study population:

As in the full population, there were more patients admitted to other units (98.2%) than ICU (1.8%). Average SAPS II score was 38.56±18.82 with a median ICU length of stay around 3 days [IQR 1, 5]. Median stay was 0 days [IQR 0, 3] with a mean of 2.6±4.76 days in non-ICU patients. ICU-admitted patients came from 323 distinct geographical centers and patients not admitted to ICU from 1239 centers around France.

Matched Study Population:

Of the 12,422,433 patients older than 64 years, propensity score matching on admission status resulted in 407,332 matched patients; 203,666 patients in each cohort. The median age was 75 years [IQR 70, 81] in ICU admitted patients and 76 years [IQR 70, 82] in non-ICU patients. After matching, a few variables had standardised differences greater than 10% including age, surgery type, cancer, and pulmonary circulation disorder, which were adjusted for in the logistic regression model. The C statistic was 0.600 after matching (before matching: C statistic 0.887). The mean propensity score for these matched patients was lower than for the unmatched patients (0.011±0.047 vs 0.85±0.10). However, the propensity score range of matched patients was wider than the unmatched patients ranging from 0.00063 to 0.99 while it was restricted to 0.56 to 0.99 in the unmatched cohort. The mean SAPS II score in the ICU-admitted group was 38.88±19.20. In addition, median ICU length of stay was 3 days [IQR 1,6] and 5 days [IQR 2, 9] in those not admitted to ICU. The most common surgery type was cardiac surgery in ICU patients (n=85,852) and orthopedic surgery (n=27,770) in the other cohort.

Table 6 reports the in-hospital outcomes for the matched cohort. Except for in-hospital mortality and heart failure, all other outcomes were rare (incidence rate <10%) and thus, relative risks were calculated in addition to odds ratios. 38,948 (19.12%) patients died after admission to ICU and 4301 (2.11%) patients died after admission to other units with a relative risk (RR) of 10.32 [95% CI 10.06 to 10.58]. Other postoperative complications were more common in those admitted to ICU with relative risk ranging from 4.24 to 13.46. Overall, postoperative complications occurred in 78,660 (38.6%) patients admitted to ICU and in 20,885 (10.3%) patients not admitted to ICU. 29,247 (14.3%) patients with at least one complication during ICU admission faced mortality whereas only 1,765 (0.86%) patients with at least one complication died when not admitted to ICU.

	ICU patients (%)	**Non-ICU patients (%)**	**Adjusted OR, 95% CI**	**RR, 95% CI**
Mortality	38,948 (19.12)	4,301 (2.11)	12.920 (12.505, 13.349)	10.322 (10.061, 10.588)
MI	7,576 (3.72)	1,595 (0.78)	4.360 (4.126, 4.607)	4.248 (4.027, 4.481)
Heart Failure	30,340 (14.90)	14,357 (7.05)	2.153 (2.107, 2.201)	1.991 (1.955, 2.029)
Stroke	6,620 (3.25)	1,363 (0.67)	5.109 (4.816, 5.419)	4.972 (4.696, 5.263)
Renal Failure	35,673 (17.52)	3,163 (1.54)	14.408 (13.881, 14.955)	11.942 (11.584, 12.310)
Sepsis	30,040 (14.75)	2,459 (1.21)	15.881 (15.229, 16.560)	13.462 (12.996, 13.941)

Table 6. *Postoperative outcomes in the older cohort*

Discussion

The primary finding of this study was that after matching patients for age, sex, hospital centers, surgery type and preoperative medical conditions, admission to ICU was associated with an increased risk of in-hospital mortality in adult patients after any surgical procedure (RR 11.53; 95% CI 11.27 to 11.79). To see if the hypothesis holds true in the older population (>64 years), we replicated the same propensity score matching model which confirmed the above stated finding (RR 10.32; 95% CI 10.06 to 10.58). The impact of ICU admission is thus considered to be similar in all patients (18 to 110 years) and in older patients (>64 years).

Assuming that postoperative complications occurred during or after ICU admission, we can conclude that ICU admission resulted in an increased risk of all postoperative complications in both the general population as well as the older cohort where sepsis had the highest risk associated with ICU admission followed by renal failure, stroke, myocardial infarction, and heart failure. Of those admitted to ICU, 32.7% with at least one of these complications died in hospital whereas only 7.8% of such patients not admitted to ICU observed mortality. However, when comparing older matched cohort to the full matched cohort, we find a 5% absolute difference in mortality of ICU-admitted patients with the older group at higher mortality (19%). On the other hand, this absolute difference in non-ICU patients is quite small (0.6%) which means that considering pre-admission variables, patients are generally better off when not admitted to ICU regardless of age. This is further confirmed when we examine deaths in those with at least one postoperative complication and find similar absolute differences.

One might attribute this to a higher postoperative severity in those admitted to ICU which could not be adjusted for. While SAPS II was available for the patients admitted in ICU, no severity clinical index was available for patients not admitted to ICU. At baseline (*i.e.* preoperative period), patients in both groups had similar characteristics which minimizes any variation in chronic medical history. This confirmed that 1 in 3 patients admitted to ICU died not because of chronic comorbidities or any other characteristics related to the patient’s chronic condition (well summarized by the covariates entered in the propensity score matching model), but perhaps due to the acute clinical medical conditions related to surgery (*e.g.* acute perioperative anemia, emergency surgical procedure, *etc.*) which we were not able to match for as they were not available in our dataset.

The results of our study are however in line with many other cohort studies that have demonstrated a high postoperative risk associated with surgical procedures in patients admitted to ICU which seems counterintuitive as close monitoring of patients in critical care is supposed to improve patients' prognosis by prompting timely treatment/intervention. A recent study on US Medicare dataset and the only matched study on this topic looking at the association between mortality and length of hospital stay in those older than 65 years undergoing surgical procedure showed a lower-survival rate in ICU discharged patients (adjusted HR 1.07; 95% CI 1.04 to 1.10).(1) Similar to our finding, another cohort study by The International Surgical Outcomes Study (ISOS) group conducted in patients from 27 countries demonstrated no survival benefit from critical care admission following elective surgery (adjusted OR 3.01; 95% CI 2.01 to 5.21).(9) In addition, there is also evidence to the contrary suggesting that an indirect ICU admission is associated with increased risk for postoperative mortality than direct ICU admission (adjusted OR 2.39; 95% CI 2.01 to 2.84). However, this can be attributed to unadjusted severity in the two groups as those admitted indirectly were likely to have a high severity of illness than those admitted directly.(10) While these studies confirm an increased mortality risk with ICU admission, there is a large gradient of risk when considered in light of different surgeries which may differ with age.

Similarly, another cohort study by the ISOS group illustrated that approximately 17% of patients developed postoperative complications following surgery and 2.8% of such patients died in hospital.(11) Our study reported estimates higher than the one reported by this study in that 21%

of the matched population developed at least one major postoperative complication and 28% of such patients died in-hospital. However, variation in these estimates might be due to slightly different baseline risk and the diversity of surgical patients included in both studies – ISOS only included elective surgical patients. In fact, studies from the USA have shown a higher mortality rate after postoperative complications ranging from 12% to 28%, similar to the results our study demonstrated.(12,13) With such high risk of complications that eventually lead to mortality, it is important to seek an answer to the question: are we admitting the right patients to ICU?

One may consider chronological age to be the culprit behind high mortality risk in older patients. In fact, age is considered a major predictor for postoperative mortality, but the literature suggests that comorbidities and clinical severity are equally as important.(14) In fact, our study considered an age- and comorbidities-matched population when analysing patients in both full and older population to minimize any variation or bias. There is little to be found in international guidelines regarding ICU admission for the elderly segment of our society that is showing a growing need of critical care and specifically, where information about their prognosis and outcome is lacking.(15) More research on ICU-related admission decisions can limit the high in-hospital mortality in this cohort and allow hospitals to create space for patients who will benefit most from this scarce but valuable resource.

This is the largest population-based matched cohort study that has assessed the association of ICU admission with in-hospital mortality and will be relevant to countries with publicly funded healthcare systems, such as Canada. The strength of our study is that it considered confounding factors like age and preoperative comorbidities thereby allowing a fair comparison between the two groups. We included a large cohort of patients undergoing any type of surgery in France with an extensive list of comorbidities to match patients. Inclusion of all surgery types over a 5-year period makes the study more pragmatic. In addition, we were able to find near-exact match in 91% of the ICU admitted patients with non-ICU patients.

Study Limitations

The findings of our study are based on measured covariates only and should be interpreted with caution due to the additional limitations mentioned henceforth. First, propensity score matching is one of the most rigorous methods for causal inference in observational studies, but it is only based on measured covariates thereby not resolving the potential of bias in terms of unmeasured covariates (residual confounding). In our study, we consider that the lack of balance for acute medical conditions biased our results significantly. Second, planned surgical procedures are associated with better postoperative outcomes than unplanned emergency procedures.(16) Again, we had no information on this aspect and so, our outcomes were considered without any categorization of planned or unplanned. While some surgery types are only performed in an emergency setting (*e.g.* open fractures, hip fractures, trauma-related surgery, *etc*.), we have to assume that our balancing score was not appropriate for this and that intervention effect estimation might have been biased. Third, mortality data was only available for those that died in the hospital at some point in time. While this could have been mitigated by using standard 30-day mortality whether in hospital or after discharge from the hospital, this information could not be accessed as mentioned previously. Fourth, there was no standard follow-up period in this population-based study leading to an absolute mean difference of 3 days between ICU (2 days) and patients admitted to other wards (5 days). This makes it difficult to interpret how in-hospital mortality differs based on a standard length of stay. However, we know that mortality (22.9%) was at its peak during the first two ICU days (≤48 hours) than in non-ICU patients where mortality (34.2%) declines sharply after the first 24 hours. Finally, while we controlled for preoperative co-morbidities, perioperative clinical severity can confound the relationship between ICU admission and in-hospital mortality. The score being used to measure clinical severity is only used in ICU admitted patients. Without any other preoperative severity metric for patients admitted to other units, clinical severity cannot be eliminated as a confounding factor. In addition, the timing of postoperative complications was unknown. In this study, we assumed that patients developed complications after admission to an ICU; however, these events could have occurred before ICU admission meriting inclusion in the propensity model.

Implications

Since a randomised trial comparing outcomes for similar patients allocated to two different wards is difficult and might be considered unethical, we have tried to do so by using propensity score matching after considering all measured covariates. Our population-based study demonstrated that when adjusting for preoperative clinical severity, patients admitted to ICU postoperatively had poor outcomes (*i.e.* increased mortality and postoperative complications) in comparison with non-ICU patients, regardless of age. A growing elderly population will require more critical care resources, and admission to ICU should be based on assessment done before surgery to assess the risk of mortality and complications. Scores like POSPOM can improve risk communication to the patient and healthcare provider while improving clinical decision making.(17) Consequently, scores that are part of admissions policies and include variables beyond chronic comorbidities, such as SAPS II (or more recent implementations), should be included in future studies to accurately assess the risk in both ICU and non-ICU populations. Further research is required to develop predictive scores that go beyond the chronic medical history and provide a better description of the patients' condition at the time of the surgical procedure.

Conclusions

Among postoperative patients in France, those admitted to ICU had a higher risk of in-hospital mortality and complications than those not admitted to ICU when only chronic medical histories are considered. ICU admission based only on these criteria might not be optimal. Further research is needed to explore the role of preoperative risk assessment in ICU admission and subsequent mortality.

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CONCLUSIONS & FUTURE DIRECTIONS

This research study focused on the role of age in admitting postoperative patients to ICU as well as the impact of ICU admission on in-hospital mortality and major postoperative complications. It found that postoperative clinical severity differs significantly between the young and the old independent of their age with the older population displaying a higher clinical severity. This signified that older patients at higher risk were being admitted to ICU so their in-hospital mortality was proportionally higher which can be due to an overestimation of their physiological reserve to bear intensive treatment. We also learnt that the younger patients demonstrated a lower clinical severity upon admission and a comparatively lower mortality rate suggesting that clinicians are able to identify patients who will benefit the most in the younger population. However, it is also likely that these patients were able to survive ICU because of a lower severity of illness. Similarly, our propensity matched study showed that ICU admission lead to a higher in-hospital mortality in patients when matched for age, sex, surgery type, and comorbidities. We can speculate that perhaps the care process from surgical theatre to ICU admission is not optimal; however, absence of perioperative acute conditions is a major limitation in our conclusion.

Exploration of frailty in the older population is needed. Studies have found that clinical severity is significantly higher in the older group (>75 years of age) independent of their age which minimizes the role of chronological age in research. However, this does not shed light into the physiological reserve a patient has to cope with intensive treatment. This potentially can be remedied by adding frailty assessment before surgery, which can highlight the risks involved. Similarly, our research focuses on clinical severity within the first 24 hours of ICU admission which hinders any insight into patients admitted to other postoperative wards in terms of clinical severity. Future research can benefit from exploring preoperative risk scores to see if patients admitted to critical care belonged to a low- or high-risk population.

APPENDIX

Age	Points
<40	0
40-59	7
60-69	12
70-74	15
75-79	16
$\geq$ 80	18

Appendix A1. *SAPS II "age" scoresheet*

1. Age
2. Heart rate
3. Systolic blood pressure
4. Body temperature
5. PaO_2/FiO_2 ratio
6. Urinary output
7. Serum urea or serum urea nitrogen level
8. WBC count
9. Serum potassium level
10. Serum sodium level
11. Serum bicarbonate level
12. Bilirubin level
13. Glasgow Coma Score
14. Type of admission
15. AIDS
16. Hematologic malignancy
17. Metastatic cancer

Appendix A2. *All variables included in SAPS II*