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Research Article

A Cox's Proportional Model to Assess Survival Prognostic Factors in Patients Over 85 Years of Age Undergoing Heart Surgery

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Abstract

Introduction: "The progressive and growing prevalence of octuagenarians (O) and over-octuagenarians (>O), susceptible to cardiac surgery has generated an ethical and economic reflection on the usefulness and opportunity to use the limited resources of intensive care for these patients. **Methods:** The primary end point of the study has been highlight any difference in post-operative and ICU mortality between patients (O) and (>O) by setting a Cox's proportional hazard model. **Results:** The 6.9% of the population studied were 85 years of age or older; therefore the over 85 yrs sub-group (≥ 85 yrs.) was 889 patients and the under 85 yrs sub-group 11966. Hospital mortality was found to be significantly higher (+4.3%) in the over 85 yrs. Factors significantly associated with postoperative hospital survival of over 85 yrs. were found to be: (i) male gender, arterial disease, COPD, pathology of the aortic and mitral valve; (ii) interaction unstable angina and common trunk obstruction, the value of the CCS scale; (iii) RBC and FFP transfusions, together with total blood loss; (iv) post-operative septic shock, acute renal failure, cerebral stroke, mechanical ventilation, ventilator associated pneumonia, and tracheostomy. **Conclusions:** Our data suggest the importance of the age variable as well as the fact that the two populations are distinct and different. A further and future multivariate analysis will be conducted with the use of propensity score matching.

Keywords: Heart surgery; Octuagenarian; Prognostic factor; Proportional hazard model

Introduction

Octogenarians (O) and ulta-octogenarians (>O) represent the fastest growing segment of the population in the Western world and over 40% of these show end stage cardiovascular disease, both coronary and valvular, susceptible to major cardiac surgery [1]. From the end of World War II until the 1970s, only about 20% of patients undergoing cardiac surgery were over the age of 40, while in the 1970s, patients considered to be "elderly" and undergoing cardiac surgery those over the age of 60 were found (5% of all interventions) [2]. In the 1980s and early 1990s, the elderly "cardio-surgical" patient was the one over the age of 70 (25% of operations) [3].

With the first decade of the 21st century, the frequency of octogenarians and ultra-octogenarians, coronary and valvulopathic patients treated with cardiac surgery, has progressively increased up to representing about 6-10% of cardiac surgery operations [4]. Recent evidence in the literature describes cardiac surgery even in ninety-year-olds [5] and beyond [6]. Patients over 80 are however susceptible to a longer length of stay in intensive care and hospital (1.5 or 2 times greater than patients under 80) [4]. In octogenarian and ultra-octogenarian patients who, due to post-operative complications, require a prolonged length of stay in ICU, mortality increases considerably and reaches values between: 31-56.5%)

[4]. Such advanced age impacts: (i) on hospitalization costs (ii) on early death [OR= 4.28, 95%CI=1.59-11.53] [9] and (OR= 6.7, 95%CI= 1.8-24.4, p = 0.004) [10]; (iiI) on 30-day mortality (3.1-21%, versus 1.6-2.2 p<0.001), although published data are conflicting [7-10,13-17].

The main predictive factors of mortality in octogenarian and ultra-octogenarian patients emerging from the analysis of the literature are NYHA > III-IV, CCS > III-IV, age (25% more for each year), previous cardiac surgery, previous cerebral stroke, preoperative chronic renal failure and postoperative acute renal failure [8], postoperative arrhythmias and sepsis, need for reoperation, chronic anemia [25]. Undoubtedly one of the alternative options to cardiac surgical revascularization could be the percutaneous route (PCI) in the angiography room by the interventional cardiologists. In this regard: in the late 80s, 30-day mortality was 8.8% after CABG and 7.4% after PCI (p=0.514). Furthermore, if major cardiac and encephalic vascular complications (MACE) can result in 35.2% in the PCI group vs. 27.9% in the CABG group (p = 0.36), overall mortality respectively (11.3% vs. 27.9% p = 0.002) [18]. Several studies confirm that off-pump CABG surgery (O-CABG) remains a valid option for myocardial revascularization, being able to optimize the outcome in elderly patients. As regards aortic valve surgery, the trans-catheter AVR technique (TAVI) was developed in order to minimize operative stress and trauma in high-risk patients, such as octogenarians and ultra-octogenarians [19,20].

While patient selection for TAVI is still a matter of debate, the overall 30-day mortality was 5.6% in the AVR cohort and 8.8% in the TAVI (p = 0.55); likewise the mortality due to cardiovascular causes equal to 3.4% and 7.6% (p=0.03), respectively. Actuarial survival at 6 months of 89.8% and 74%, respectively in patients undergoing TAVI and AVR. [20].

Finally, there is little evidence on quality of life after surgery [18,32], showing that four years after surgery, 95.2% of octogenarians live alone, with a partner or with relatives , and only 4.0% require permanent home nursing care. Functional capacity emerged to be on average high, and with no significant difference between under and over 80s (< 80: 87 ± 22 and < 80: 67 ± 31, p = 0.108).

To date, despite the evidence in the literature, coronary heart and valve surgery still appears to have a controversial indication in patients over the age of 80. In this context, it was considered useful to analyze all the cases present in the electronic database of the Post-Operative Intensive Care Unit of the Luigi Sacco Hospital, in order to produce new knowledge in the context of this "hot topic".

Methods

Aim of the study

Given the fact that this topic still presents controversial points and given the progressive increase in the age population especially in our country, although cardiovascular pathologies are progressively decreasing both in terms of coronary and valvular pathology, we believe it is necessary to conduct a retrospective study, observational, single-center in order to establish whether there is a difference in survival between over 85 and under 85 who undergo cardiac surgery; as well as the prognostic factors predictive of the same survival, in the context of patients undergoing cardiac surgery at the Clinical Division of Cardiac Surgery of the Luigi Sacco Hospital, admitted to the post-operative Intensive Care Unit (TIPO) of the same Company, for the post-operative -operative.

Objectives of the study

Primary Objective of the Study

- Highlight any difference in post-operative and ICU mortality between patients (O) and (>O) - stratified in a single age class indicated as group (H) (> = 85 years) and younger patients (< 85 years)
- Mortality data will also be stratified on the basis of the type of intervention (coronary, valvular, combined, aortic); if the sample size allows it, the valve interventions will be stratified in terms of mono, bi, tri-valve interventions; as well as the difference in mortality over time will be evaluated, stratifying patients into groups of 5 years starting from 1999, up to 31-12-2019.

Secondary Objective of the Study

- A multivariate proportional hazards survival model (Cox model) will be constructed, which will identify the survival predictors of the individual age groups and which has as its outcome (dichotomous dependent variable the patient's hospital mortality: 1= yes (alive); 0 = no (dead). Two models will be constructed, one with age as the continuous quantitative independent predictive variable, one with age considered as the dichotomous categorical independent predictive variable (1= > 80 years, 0 = ≤ 80 The additional independent predictive variables will be identified as: (i) demographic (ii) anamnestic (iii) intra-operative (iv) post-operative and hospitalization in TYPE (see, paragraph variables).

Study type and design

Single-center prospective observational study

Study Center: The centers where the retrospective observational study will be carried out are (i) Clinical Division of Cardio Surgery (ii) Post-Operative Intensive Care, of the Luigi Sacco Hospital, University of Milan.

Study population

The study population of interest consists of all patients aged > 80 years undergoing cardiac (i) coronary (ii) valvular (iii) combined valvular + coronary (iv) aortic surgery and heart defects, from 01- 01-1999 to 31-12-2019.

Inclusion criteria: patients aged ≥ 85 years

Exclusion Criteria: None

Variables

The dependent predictor variable considered for the model is survival in hospital (categorical/dichotomous: alive=1, dead=0). The independent predictor variables considered for the model are:

- **Demographics:** gender (male/female), age, BMI,
- **Risk Factors:** (presence yes = 1): diabetes (yes/no), hypertension (yes/no), arterial disease (yes/no), chronic renal failure (yes/no), chronic obstructive pulmonary disease (COPD) (yes/no); type of preoperative heart disease coronary artery disease (CAD) (yes/no), aortic disease (stenosis or regurgitation or both) (yes/no), mitral valve disease (stenosis or regurgitation or both) (yes/no), tricuspid disease (stenosis or insufficiency or both); CAD + valve disease (yes/no), redo surgery (yes/no), emergency surgery (yes/no); pre-operative risk score (yes: > of the specific cut-off): NYHA (yes, >2; no, ≤2), CCS (yes, >2; no, ≤2), CRS (yes, >8; no, 8), Euro-Score; left ventricular function assessed on left ventricular ejection fraction (LVEF yes, ≤30%; no, >30%).
- **Intra-operative variables:** CPB time, extracorporeal circulation time, ACC time, circulation arrest time, IT time, duration of surgery, number of transfusions of RBC erythrocytes and FFP plasma, use of vasoactive drugs (i.e. dobutamine, dopamine, epinephrine). We merged the NYHA (for CVD) and CCS; to be considered quantitative continuous/discrete or categorizable in dichotomous depending on the cut-off to be established after the descriptive analysis.
- **Post-operative / TYPE variables:** duration of artificial ventilation (MV) in hours, use of vasoactive drugs (i.e. dobutamine, dopamine, epinephrine), development of organ failure (i.e.=kidney, heart, lung, pH), tracheostomy ; development of infections/sepsis, development of non-infectious non-organ complications.

Sample size

The sample of the population is represented by patients admitted to the Clinical Division of Cardiac Surgery of the Luigi Sacco Hospital, in twenty years, from 01-01-1999 to 31-12-2019.

Ethical aspects

Although a retrospective observational study: The procedures reported in the study regarding the conduct, execution and documentation comply with the ethical principles set out in the Declaration of Helsinki and its revisions. The study will be conducted taking into account regulatory requirements and legal obligations, with the approval of Ethic Committee of ASST Fatebenefratelli Sacco.

Furthermore: Access to the database, consisting of sensitive as well as clinical data, will be reserved only for the researchers who conceived the study. The processing of personal data will be anonymous and aggregated, in accordance with law 675/1996 and law 196/03 on the protection of.

Statistical analysis

The above data were progressively and prospectively entered into an electronic relational database equipped with logical adequacy checks by TIPO staff, once the patients were discharged from the hospital.

Statistical analysis will be conducted with STATA 12.1. Student's t-test will be used for the analysis of quantitative variables; non-parametric tests will be applied if the distribution of the values of the variables does not follow a normal trend. For comparison of categorical variables, the X^2 test will be used with correction of Fisher's exact test, if necessary (expected values <5). Kaplan Meier survival analysis will be applied to compare patient survival in individual age groups and/or type of surgery. The multivariate model of survival analysis with Cox proportional hazards was used for the identification of outcome predictors (yes/no survival).

Results

The 6.9% of the population studied were 85 years of age or older; therefore the over 85 yrs sub-group (≥ 85 yrs.) was 889 patients and the under 85 yrs sub-group 11966. In the over 85s there was an equal distribution between genders (M:F = 1.1 : 1), while among the under 85s the M:F ratio was 2.4 : 1 (M= 70.6% and F = 29.4%). The mean age (SD) of the under 85 yrs was respectively equal to 63.91 (±11.1) and equal to 87.2 (±15.6) for Pts ≥ 85.

Comparison between under 85 yrs and over 85

The characteristics related to the pre-intra-post-operative variables are summarized in Tables 1-3. An occurrence of hypertension, arterial disease, coronary artery disease and severe renal insufficiency as well as re-operations was found to be significantly higher among the over 85s and under 85s respectively (Table 1). Likewise, the peri-operative risk scores (NYHA, CCS, CRS) were on average significantly higher in the over 85 group than in the under 85 group.

	Total Population (12855)	Under 85 (n=11966)	Over 85 (n=889)	Test (**)	p-value
Diabetes n (%)	2751 (21.4)	2564 (21.4)	187 (21)	0.0761	0.783
Hypertension, n (%)	6913 (53.8)	6324 (52.9)	318 (34.9)	**50.47**	**<0.001**
COPD n (%)	1413 (11)	1296 (10.8)	117 (13.2)	**4.36**	**0.032**
Chronic renal failure n (%)	1276 (9.9)	1106 (9.2)	170 (19.1)	**74.45**	**<0.001**
Arteriopathy, n (%)	2944 (22.9)	2612 (21.8)	332 (37.3)	**101.49**	**<0.001**
Endocarditis, n (%)	24 (01.9)	232 (1.9)	8 (0.9)	**5.93**	**0.015**
Unstable Angina, n (%)	1192 (9.2)	1082 (9)	99 (11.1)	**4.11**	**0.012**
Common Trunk, n (%)	1696 (13.2)	1541 (12.9)	155 (17.4)	**13.91**	**<0.001**
RE-operation n (%)	765 (6)	738 (6.2)	27 (3)	**17.27**	**<0.001**
PTCA, n (%)	59 (0.5)	58 (0.5)	1 (0.1)	3.52	0.060
Pre-surgery Cardiogenic Shock, n (%)	107 (0.8)	104 (0.9)	3 (0.3)	3.59	0.058
Heart Pathology, n (%):					
• **CAD**	8350	7858 (65.6)	492 (55.3)		
• **Aortic Valve**	2459	2185 (18.3)	274 (30.4)		
• **Mitralic Valve**	2315	2179 (18.2)	136 (15.3)	**76.78**	**p<0.0001**
• **Tricuspidal Valve**	487	437 (3.7)	30 (0.4)		
• **Pathology of the Aorta**	111	94 (0.8)	17 (1.9)		
EF (%), mean (SD)	49.7 (13.5)	49.7 (13.6	50 (11.1)	-0.609	0.524
NYHA score, (#), median (IQR)	2 (1-3)	2 (1-3)	3 (2-3)	**-9.873**	**<0.001**
CCS, (#), median (IQR)	2 (1-3)	2.01 (0.982) / 2 (1-3)	2.63 (0.945) / 2 (2-3)	**-6.376**	**<0.001**
CRS, median (IQR)	4 (2-6)	4 (2-6)	7 (5-9)	**-24.976**	**<0.001**

*SD: standard deviation; IQR=Interquartile range in case of non-normal distribution of the variable; (**) the column represents the Chi-square value (or Fisher's exact test) for qualitative variables and Student's t for quantitative ones.

Table 1: Summary of pre-operative variables and comparison between over 85 and under 85*.

The type of intervention was found to differ between the two populations (Table 2). Specifically, operations for valvular disease and CABG were significantly more frequent among the over 85s than in the under 85s, where there was a greater (+18%) use of extracorporeal circulation. Conversely, among Pts ≥ 85 there was a shorter total duration of the operation, although blood losses and the need for blood transfusions were greater. The analysis of postoperative variables revealed a significantly higher frequency of cardiogenic shock, acute renal failure and ventilator-associated pneumonia occurring in the over 85 yrs. compared to under 85 yrs. compared to the duration of artificial ventilation, hospital stay and in TYPE (post-operative intensive care) substantially superimposable among the populations.

	Total Population (12855)	**Under r85** (n=11966)	**Over 85** (n=889)	**Test (**)**	**p-value**
Surgery Type n (%):					
• CABG	7087 (55.1)	6725 (56.2)	362 (40.7)		
• Valve Replacement (VR)	1307 (10.2)	1174 (9.8)	133 (15)		
• CABG + VR	3060 (23.8)	2812 (23.5)	248 (27.9)	**100.78**	**0.002**
• Aorta Surgery (Thoracic)	280 (2.2)	239 (2)	41 (4.6)		
• Other Surgery	1121(8.7)	1016 (8.5)	105 (11.4)		
ECC# (si/no) , n (%)	1095 (78.5)	9546 (79.8)	549 (61.8)	**189.9**	**<0.001**
Intra-operative Cardiogenic (%)	394 (3.1)	360 (3.2)	34 (4.1)	2.22	0.136
Surgery Duration minutes, median (IQR)	270' (240'-320')	275' (240'-325')	265' (210'-310')	**6.218**	**0.011**
Aortic Clamping durata in minuti, mediana (IQR)	71' (53'-95')	71 (53-95)	70 (53-94)	-0.641	0.489
EEC Duration minutes, median (IQR)	105' (82'-135')	105 (82-135)	99 (79-126)	0.504	0.590
Intra-operative Minimal Temperature, median (IQR)	31.6 (2.8)	31.6 (2.7)	31.7 (2.8)	-0.431	0.660
RBC Trasfusion (#), median (IQR)	1 (0-3)	1 (0-3)	2 (1-4)	**-7.620**	**<0.001**
FFP Trasfusion (#), mediana (IQR)	1 (0-2)	1(0-2)	1 (0-3)	-0.020	0.317
Blood Loss ml, median (IQR)	500 (330-800)	500 (340-750)	600(300-900)	**-2.463**	**0.013**

EEC: extracorporeal circulation; *SD: standard deviation; IQR=Interquartile range in case of non-normal distribution of the variable; (**) the column represents the Chi-square value (or Fisher's exact test) for qualitative variables and Student's t for quantitative ones.

Table 2: Summary of intra-operative variables and comparison between over 85 and under 85*.

	Total Population (12855)	**Under 85** (n=11966)	**Over 85** (n=889)	**Test (**)**	**p-value**
Post-operative Cardiogenic Shock n (%)	880 (6.8)	792 (6.6)	88 (9.9)	**12.49**	**<0.001**
Post-operative Acute Renal Failure, n (%)	1452 (11.3)	1275 (10.7)	177 (19.9)	**60.15**	**<0.001**
Post-operative Septic Shock, n (%)	1060 (.8)	98 (0.8)	8 (0.9)	0.064	0.850
Post-operative Ictus Cerebri, (%)	69 (0.5)	62 (0.5)	7 (0.8)	0.992	0.319
Mediastinitis, n (%)	48 (0.4)	45 (0.4)	3 (0.3)	1	0.856
Post-operative Hepatic Failure n (%)	325 (2.5)	299 (2.5)	26 (2.9)	0.582	0.445
VAP, n (%)	106 (3)	958 (8)	105 (11.8)	**14.22**	**<0.001**
Tracheostomy n (%)	323 (2. 5)	294 (2.6)	29 (3.3)	2.018	0.165
Mechanical Ventilation (hrs.)	13(9-20)	12 (9-19)	15 (11-22)	-3.008	0.460
LOS in Post-Surgical ICU (days), median (IQR)	2(1-3)	2 (1-3)	2 (1-3)	-1.685	0.484
LOS in Hospital (days), median (IQR)	12(9-15)	12 (9-15)	12 (9-16)	0.284	0.503

*SD: standard deviation; IQR=Interquartile range in case of non-normal distribution of the variable; (**) the column represents the Chi-square value (or Fisher's exact test) for qualitative variables and Student's t for quantitative ones. LOS: Length of stay; VAP = Ventilator Associated Pneumonia

Table 3: Summary of post-operative variables and comparison between over 85 and under 85*.

Hospital mortality

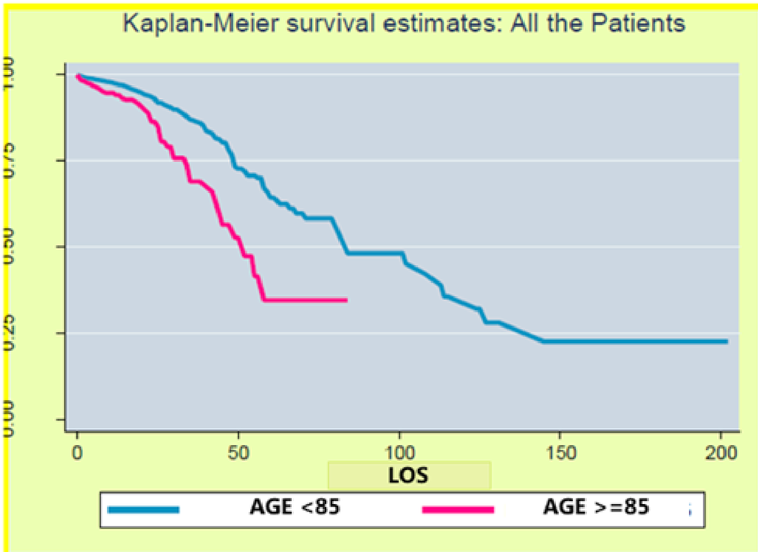
Hospital mortality was found to be significantly higher (+4.3%) in the over 85 yrs. The cumulative incidence of this data is also confirmed after the stratification by type of intervention as shown in Table 4. Hospital mortality was found to be higher, resulting higher in valvular, combined and aortic surgery.

Survival between the two defined groups of patients was significantly higher in Pts < 85 yrs (Figure 1). Stratifying by type of intervention, this trend is confirmed (Figures 2-5). The under 85s were found to have a survival from cardiac surgery significantly higher than that of the over 85 yrs. (Figure 1). This pattern was also found in cardiac surgery by analyzing the two populations within the type of surgery (Figures 2-5). Those over 85 who underwent valve replacement surgery were found to have a lower hospital survival than those who underwent other types of surgery such as can be seen from Figure 6. While in the under 85s survival was comparable between the different types of cardiac surgery up to about 50 days (Figure 7): precisely those with CABG surgery and valve replacement were found to have a longer survival.

	Under 85		Over 85		
	N	n (%)	N	n (%)	p-value
Total Population	11966	465 (3.9)	889	73 (8.2)	0.001
Surgery Type					
• **CABG**	6725	180 (2.7)	362	20 (5.1)	0.003
• **VR**	1174	94 (8)	133	16 (12)	0.082
• **CABG + VR**	2812	248	124 (4.4)	23 (9.3)	0.001
• **Aorta Surgery (Thoracic)**	239	25 (10.5)	41	10 (24.4)	0.017
• **Other Surgery**	1016	42 (4.1)	105	4 (3.8)	0.565

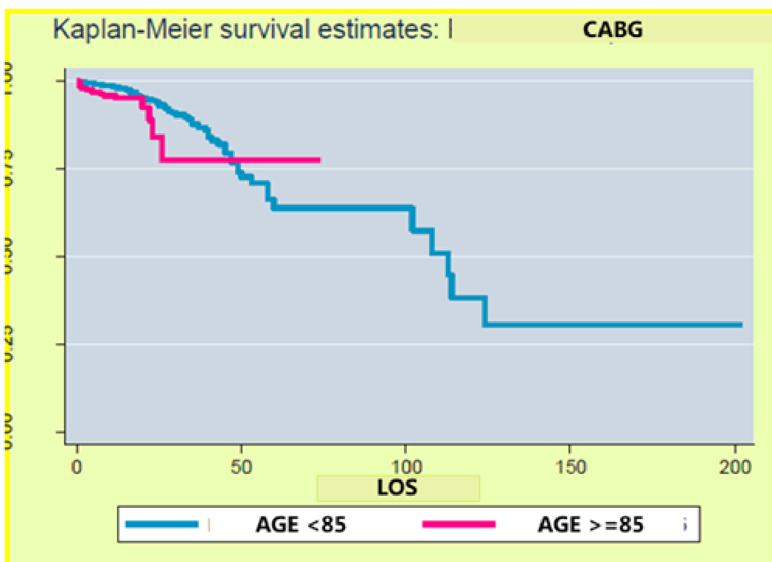
The cumulative incidence was reported separately by type of intervention. The last column shows the significance level of the Chi-squared test. [number of deaths (n) and cumulative incidence (%)) and comparison between over 85 and under 85. The same comparison was also reported within type of intervention]

Table 4: Cumulative incidence of hospital mortality in under 85 and over 85.



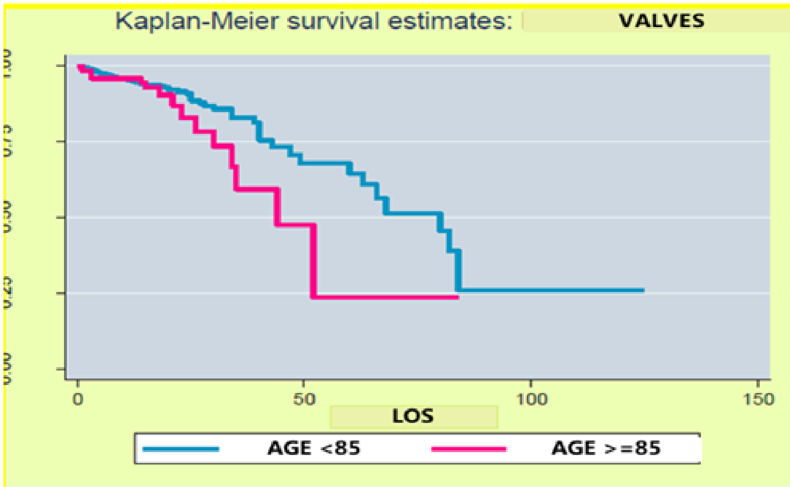
	Chi Square	p-value
Log Rank	34.09	<0.001
Wilcoxon	35.44	<0.001
Peto Peto	74.33	<0.001
Taron Ware	37.79	<0.001

Figure 1: Cumulative survival curves after Kaplan Meier's intervention: comparison between over 85 and under 85. The tests with the relative levels of significance.



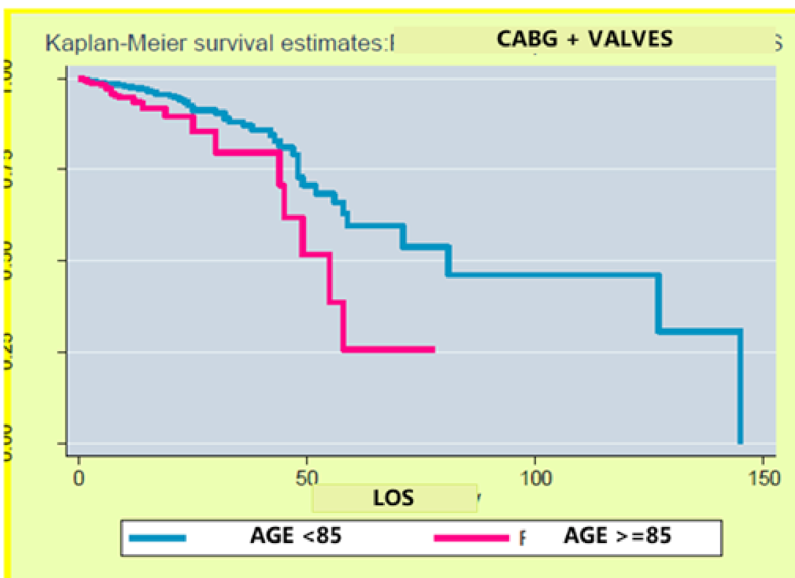
	Chi Square	p-value
Log Rank	19.65	<0.001
Wilcoxon	18.67	<0.001
Peto Peto	26.22	<0.001
Taron Ware	18.69	<0.001

Figure 2: Cumulative survival curves after Kaplan Meier intervention: comparison between over 85 and under 85, for CABG intervention.



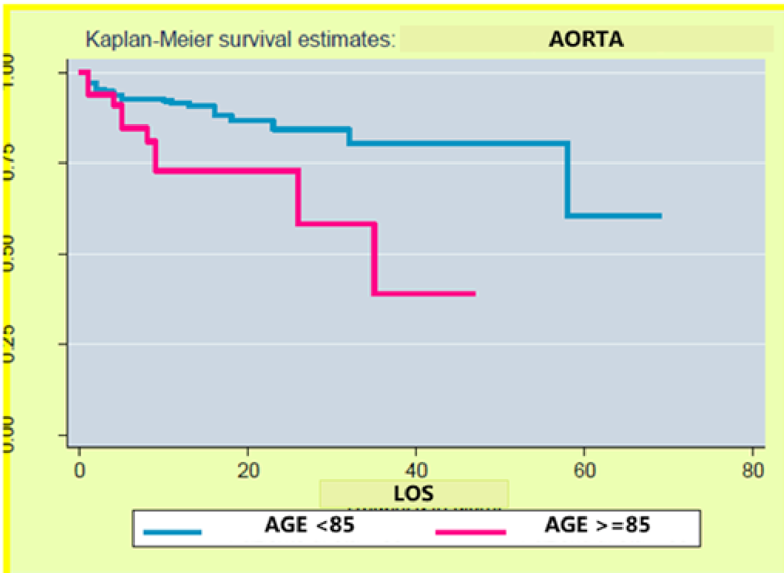
	Chi Square	p-value
Log Rank	23.52	<0.001
Wilcoxon	34.68	<0.001
Peto Peto	29.17	<0.001
Taron Ware	35.76	<0.001

Figure 3: Cumulative survival curves after Kaplan Meier surgery: comparison between over 85 and under 85, for valve replacement surgery.



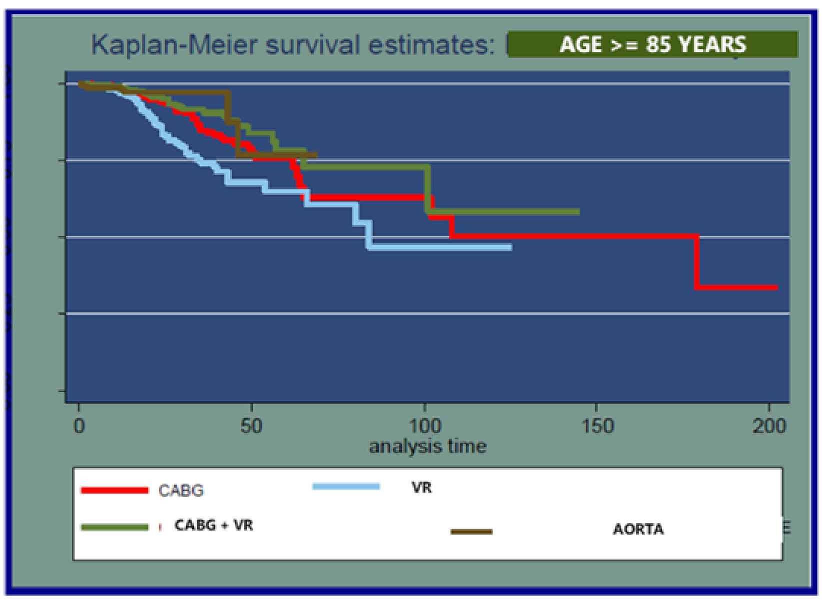
	Chi Square	p-value
Log Rank	23.52	<0.001
Wilcoxon	34.68	<0.001
Peto Peto	29.17	<0.001
Taron Ware	35.76	<0.001

Figure 4: Cumulative survival curves after Kaplan Meier intervention: comparison between over 85 and under 85, for CABG intervention + Valve Replacement.



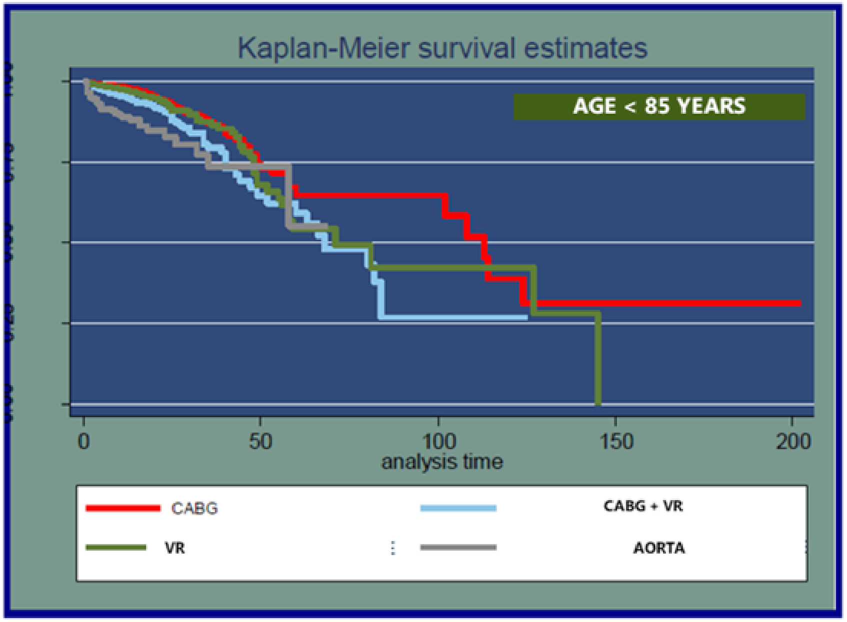
	Chi Square	p-value
Log Rank	7.94	0.005
Wilcoxon	14.26	0.0002
Peto Peto	12.89	0.0003
Taron Ware	14.42	0.0001

Figure 5: Cumulative survival curves after Kaplan Meier surgery: comparison between over 85 and under 85, for AORTA surgery.



	Chi Square	p-value
Log Rank	18.73	0.0009
Wilcoxon	57.48	<0.0001
Peto Peto	24.07	0.0001
Taron Ware	48.78	<0.0001

Figure 6: Comparison of Kaplan Meier postoperative cumulative survival curves: type of surgery within under 85 yrs.



	Chi Square	p-value
Log Rank	29.36	<0.0001
Wilcoxon	110.52	<0.0001
Peto Peto	38.06	<0.0001
Taron Ware	83.99	<0.0001

Figure 7: Comparison of Kaplan Meier cumulative postoperative survival curves: type of surgery within over 85 yrs.

Multivariate analysis

From the multivariate analysis, a higher risk of post-operative hospital death always emerged in the over 85s, compared to the under 85s (HR = 1.58), but adjusting from the point of view of risk and prognostic factors it is no longer relevant from a point of view statistical view. Factors significantly associated with postoperative hospital survival were: (Table 5)

a) Preoperative chronic renal failure

b) Arterial disease

c) Pathology of the aortic valve

d) Preoperative cardiogenic shock

e) Aortic clamping time

f) Extracorporeal circulation time

g) Total blood loss

h) Postoperative cardiogenic shock

i) Post-operative septic shock

j) Acute postoperative liver failure

k) Ventilator associated pneumonia

Variables	Total Population		Patients with Age > = 85		Patients with Age < 85	
	HR (95% C.I.)	p-value	HR (95% C.I.)	p-value	HR (95% C.I.)	p-value
	Pre-Surgery Variables					
Age: ≥85 or < 85 anni	1.6 (0.8-2.9)	0.156	/	/	/	/
Gender: Male : Femail	0.8 (0.7-1.1)	0.300	**1.2 (1.1-1.3)**	**0.027**	0.9 (0.8-1.1)	0.733
Diabetes (yes/no)	0.9 (0.6-1.4)	0.863	0.9 (0.8-0.9)	0.003	0.8 (0.6-1.3)	0.505
Chronic Renal Failure (yes/no)	**1.8 (1.2-2.9)**	**0.012**	0 .9 (0.8-1.1)	0.275	0.8 (0.5-1.2)	0.261
Arteriopathy (yes/no)	**2.1 (1.4 -3.1)**	**<0.0001**	**0.8 (0.8-0.9)**	**0.001**	0.7 (0.5-1.1)	0.056
Hypertension (yes/no)	0.7 (0.5-1.1)	0.172	1.1 (0.9-1.1)	0.325	**1.6 (1.2-2.2)**	**0.006**
COPD (yes/no)	1.1 (0.7-1.8)	0.588	**1.2 (1.1-1.3)**	**0.004**	1.2 (0.6-1.6)	0.861
Aortic Pathology (yes/no)	**2.5 (1.5-4.3)**	**0.001**	**1.2 (1.1-1.4)**	**0.011**	0 .7 (0.4-1.1)	0.078
Mitralic Pathology (yes/no)	1.1 (0.6-1.9)	0.772	**1.4 (1.3-1.6)**	**<0.0001**	0 .8 (0.4-1.5)	0.568
Tricuspidal Pathology (yes/no)	1.6 (0.5-5.7)	0.413	1.1 (0.7-1.4)	0.871	0 .6(0.1-5.2)	0.670
Unstable Angina *Common Trunk	1.9 (0.9-3.9)	0.070	**1.2 (1.1-1.4)**	**0.009**	1.5 (0.8- 2.6)	0.161
Recurrence (yes/no)	1.1 (0.5-2.5)	0.841	0.9 (0.7-1.1)	0.179	0 .5 (0.1- 4.2)	0.509
Aorta Pathology (yes/no)	2.1 (0.2-19.8)	0.520	0.7 (0.2-1.7)	0.412	–	---
EF (yes/no)	0.9 (0.9-1.1)	0.427	1.1 (0.9-1.1)	0.213	0.9 (0.9-1.1)	0.877
CCS score (#)	1.1 (0.8-1.3)	0.581	**1.2 (1.1-1.3)**	**<0.0001**	1.1 (0.8-1.2)	0.753
CRS score (#)	1.1 (0.9-1.1)	0.087	0.9 (0.9-1.1)	0.513	0 .9 (0.9-1.1)	0.877
Pre-surgery Cardiogenic Shock (yes/no)	**7.6 (2.3-25.1)**	**0.001**	1.4 (0.9-2.1)	0.093	**6.1 (1.8-12.6)**	**0.021**
	Intra-Surgery Variables					
Surgery Duration: minutes	1.1 (0.9-1.1)	0.550	0.9 (1.0-1.1)	0.149	0 .9 (0.9-1.1)	0.298
Aorta Clamping Duration: minutes	**0.9 (0.8-0.9)**	**0.002**	1.1 (0.9-1.1)	0.458	1.1 (0.9-1.2)	0.412
EEC Duration: minutes	**1.1 (1.1-1.2)**	**<0.0001**	1.1 (0.9-1.1)	0.946	1.1 (0.9-1.2)	0.435
RBC Transfusions #	1.1 (0.9-1.1)	0.189	**1.1 (1.1-1.3)**	**0.040**	0.9 (0.8-1.0)	0.478
FFP Transfusions #	0.9 (0.9-1.1)	0.198	**1.1 (1.1-1.4)**	**0.001**	1.1 (0.9-1.2)	0.253
Intra-operative Cardiogenic Shock (yes/no)	2.1 (0.7-5.8)	0.202	1.2 (0.7-1.5)	0.688	1.1 (0 .1- 8.8)	0.979
Blood Loss ml	**1.2 (1.1-1.3)**	**0.003**	**1.2 (1.1-1.4)**	**0.001**	0.9 (0.9-1.1)	0.315

Post-Surgery Variables						
Post-surgery Cardiogenic Shock (yes/no)	**0.3 (0.1-0.9)**	**0.046**	1.2 (0.8-1.7)	0.310	0.8 (0.1-9.1)	0.893
Post-surgery Septic Shock (yes/no)	**5.4 (2.5-11.9)**	**<0.0001**	**2.9 (1.8-4.9)**	**<0.0001**	---	----
Acute Renal Failure (yes/no)	1.3 (0.8-2.2)	0.341	**1.2 (1.1-1.3)**	**0.003**	0 .7 (0.5-1.1)	0.120
Acute Hepatic Failure (yes/no)	**3.969(2.2-7.2)**	**<0.0001**	1.1 (0.8-1.4)	0.454	1.3 (0.4-4.1)	0.603
Ictus Cerebri (yes/no)	0.5 (0.1-2.3)	0.376	**2.3 (1.4-3.8)**	**0.001**	1.3 (0.3-7.1)	0.770
Mechanical Ventilation Duration (hrs.)	0.9 (0.1-2.3)	0.674	**1.2 (1.1-1.5)**	**0.001**	0.9 (0.9-1.1)	0.714
VAP (yes/no)	**1.1 (0.6- 2.1)**	**0.022**	**1.9 (1.6-2.2)**	**<0.001**	0.5 (0.2-1.1)	0.089
Tracheostomy (yes/no)	0.6 (0.2-1.5)	0.276	**1.7 (1.1-2.5)**	**0.008**	0.11 (0.03-3.7)	0.217

Table 5: Cox's Proportional Hazards Models.

Precisely all the explanatory factors introduced in the Cox model being equal, the risk of incurring post-intervention hospital mortality was:

- Approximately double in those with CKD compared with those without (HR=1.8)
- Approximately double in patients with arterial disease than in those without (HR = 2.1)
- Two and a half times larger in those who had aortic disease than in those without (HR=2.5)
- Nearly 8 times higher in patients with preoperative cardiogenic shock than in those without (HR = 7.7)

Inversely associated with clamping of the aorta

- Grow by about 2% in relation to blood loss
- Five times greater in patients with postoperative septic shock than in those without (HR = 5.4)
- Approximately 4 times greater in the case of acute liver failure vs no (HR=3.97)
- 13% higher if ventilator-associated pneumonia occurred compared to no occurrence (HR = 1.13)

Figures 8 and 9 graphically show the predicted survival and the predicted hazard from the Cox model. From the analysis of the factors associated with post-operative hospital survival in the over 85 separately from the under 85s it emerged that:

1. Factors significantly associated with postoperative hospital survival of over 85 yrs. were found to be: (Table 6)

a) Male gender

b) Arterial disease

c) COPD

d) Pathology of the aortic valve

e) Pathology of the mitral valve

f) The interaction Unstable angina *Common trunk

g) The value of the CCS scale

h) Transfusions of GRC

i) Transfusions of PFC

j) Total blood loss

k) Post-operative septic shock

l) Post-operative acute renal failure

m) Cerebral stroke

n) Hours of artificial ventilation

o) Ventilator associated pneumonia

p) Tracheostomy

2. Factors significantly associated with post-operative hospital survival of the under 85s were: (Table 7)

a. Hypertension

b. Preoperative cardiogenic shock

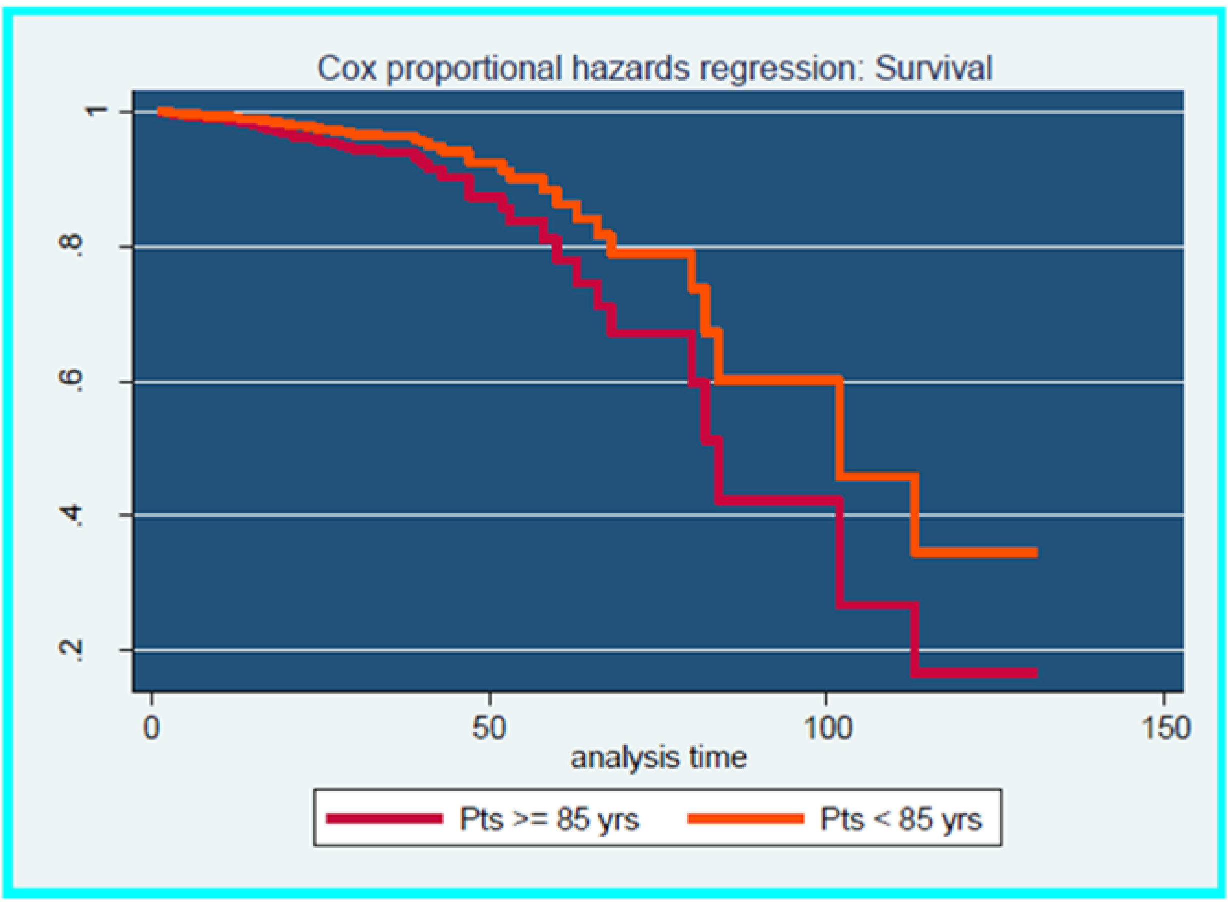


Figure 8: Estimated survival to postoperative hospital death predicted by the Cox model.

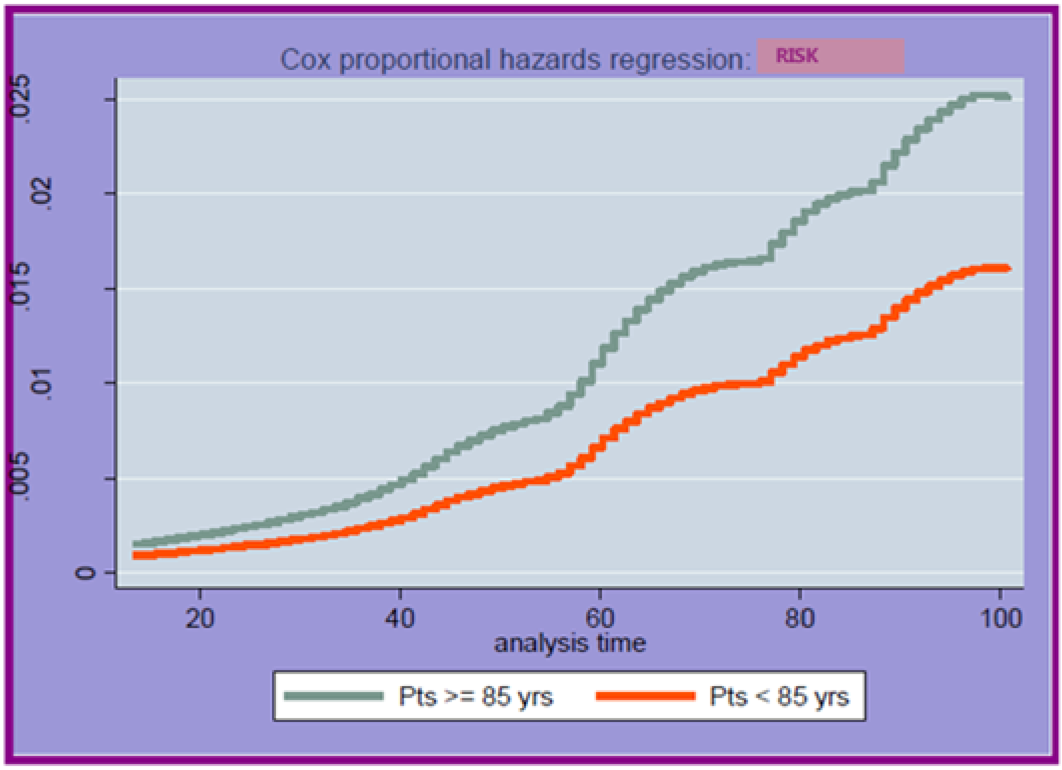


Figure 9: Post-operative hospital mortality hazard estimated by Cox's model.f

Discussion

The progressive and growing prevalence of O and >O, susceptible to cardiac surgery has generated an ethical and economic reflection on the usefulness and opportunity to use the limited resources of intensive care for these patients, giving rise to controversial opinions on the matter, as there are no clear indications in literature. Consequently, cardiac surgery for O and > O still represents a resource whose rationalized use is not yet globally shared, especially with regard to the increase in less invasive techniques offered by interventional cardiology. The main results of this study can be summarized as follows:

The over 85s differ from the under 85s with respect to the presence of some pre-operative variables such as hypertension, renal insufficiency, arterial disease, unstable angina, pathology of the common coronary artery, pathology of the aortic valve and in addition other risk scores such as NYHA, CCS, CRS. There are few differences in the intra-operative variables (intervention duration and blood loss in the over 85s; only post-operative cardiogenic and septic shock, acute liver failure and the development of VAP are more frequent in the over 85s. Survival after hospitalization post-operative is significantly higher in the under 85s both in general and in relation to the type of intervention.

Factors found to be independently and significantly associated with the risk of postoperative hospital death in the general population are: preoperative chronic renal failure, arterial disease, aortic valve disease, preoperative cardiogenic shock, aortic clamping time, extracorporeal circulation time total blood loss, postoperative cardiogenic shock, postoperative septic shock, postoperative acute hepatic failure, ventilator-associated pneumonia.

Stratifying the data according to the two groups of over and under 85 years of age, it appears that the predictive factors of mortality in the under 85s are: male gender, arterial disease, COPD, aortic valve disease, mitral valve disease, The interaction Unstable angina and the presence of left main occlusion, CCS scale value, RBC transfusions, FFP transfusions, total blood loss, post-operative septic shock, post-operative acute renal failure, stroke, hours of artificial ventilation, VAP, tracheostomy, epiphenomenon of a prolongation of artificial ventilation

This was confirmed by the data already present in the literature where it was highlighted that the post-operative course of >85 could be complicated by a prolonged period of artificial ventilation (> 48 hours) in 3.4-12.4% of cases [11,12]; (ii) a higher occurrence of dialysis-dependent acute renal failure (4.9-11.7% vs 5.4%, nons.); (iii) a more frequent postoperative decline in glomerular filtration rate (<25%): 40% vs. 30%, p = 0.02) [11-13], (iii) a higher incidence of brady-severe arrhythmias; (iv) a persistence/occurrence of severely reduced left ventricular function (OR= 8.0, 95%CI= 1.2-53.5, p = 0.032) [10]; (v) a higher incidence of postoperative neurological strokes (ischemic or haemorrhagic strokes, after heart-lung bypass) (1.8-3.6% vs. <1%) [11]. Octogenarians and ultra-octogenarians have a higher likelihood of intraoperative blood transfusion (51% vs. 30%, p < 0.001). Furthermore, if among patients aged < 85 years, chronic anemia can significantly increase the risk of early death (HR=2.03; 95%CI= 1.47, 2.80), but not of late death (OR=1.21, 95%CI= 0.88, 1.67), in >85 this does not happen (early death: HR= 1.47, 95%CI= 0.84-2.56; late death: HR= 0.92 95%CI=0.50-1.69) [14]. While among the predictive factors of mortality in the under 85s are: hypertension and pre-operative cardiogenic shock (Table 5).

Patients over 85 represent 6-10% of patients undergoing cardiac surgery [5]. In this context, the present study may be a harbinger of discussion points in the scientific community, although its observational and retrospective nature represents a possible methodological weakness. The octogenarian and ultra-octogenarian patient has a one-year survival between 90.1-95% d not significantly different from that found in patients <80 years (98%) [9,16-18]; (ii) at 3 years it is equal to 72.9-81.4%, decreasing compared to younger patients, where it is still around 94.5%) [9]; (iii) at 5 years it is 53-77.2% and in the under 80s it is 83.1%) [16,17], (iv) at 10 years it decreases to 27%. There is essentially no specific difference with our data except for a slightly higher mortality (Table 4).

In octogenarians and ultra-octogenarians, survival is strongly influenced or worsened by the process of advanced physiological aging and by the presence of other comorbidities typical of advanced age [17,18]. However, short- to medium-term mortality in the cardiac surgery population did not differ significantly between the different types of surgery [CABG: 5.1%, valve replacement: 7.6%, p = 0.51) [8]: among patients over octogenarians, hospital survival is similar, once stratified by type of intervention (coronary or valvular) [8,19]. In our series, only aortic surgery shows a significant increased mortality, probably linked to an increase in emergency operations. Gender does not have a significant impact and at 5 years mortality is not significantly different between males and females, although higher in (8.0% vs. 5.9%, p = 0.332) [11,21]. The lack of differences in early death odds of postoperative hospital death that emerges from our study is in agreement with what was found by Abel and colleagues in octogenarians [8] and by Kurlansky et al. [1], on the contrary, contrasts with that found by Kamiya et all [10]. It is difficult to explain why an initial greater survival of the under 85s and therefore less risk then loses significance. De facto, the best interpretation may be that the two groups of patients under and over 85 years of age represent a different population with respect to the age factor which divides them. This parameter is certainly confused by the effects of the clinical comorbidities of the intra-operative and post-operative variables, but does not interact with them.

It is obvious that, speaking of octogenarian and ultra-octogenarian patients, this survival is strongly influenced or worsened by the process of advanced physiological aging and by the co-presence of other comorbidities, correlated with advanced age [22,23]. In analogy with the literature [8,24] hospital survival is similar, once stratified by type of intervention (coronary or valve) [8,24]. The present study also confirms that gender does not have a significant impact on hospital mortality [11,20].

The fact that the pre-operative presence of chronic renal failure increases the risk of early death differs from the literature, while in the studies in which it was evaluated they found a greater occurrence of dialysis-dependent acute renal failure (4.9-11.7 % vs 5.4%, not significant); a more frequent postoperative decline in glomerular filtration rate (<25%): 40 vs. 30%, p = 0.02) [12-14].

Likewise with regard to pre-operative cardiogenic shock, it is understandable how the presence of severe cardiac pump impairment - and pre- and post-operative, requiring pharmacological support and with IABP, can influence the outcome and the intrinsic mortality related to cardiogenic shock itself, as well as worsening of chronic renal insufficiency or the onset of acute new renal failure. On the other hand, the literature confirms that in the over 85 yrs there is a persistence/appearance of a severely reduced left ventricular function (OR 8.0, 95% CI 1.2-53.5, p = 0.032) [10].

Our study shows a result opposite to consolidated evidence in the literature, i.e. that people over 85 undergo a prolonged (> 48 hours) period of artificial ventilation more frequently in 3.4-12.4% of cases [11,12]; on the other hand, the risk of VAP is significantly greater than what is known, although the risk of VAP is directly proportional to the increase in the time of artificial ventilation of patients.

Another point of discontinuity with the evidence [11] is the fact that a higher incidence of postoperative neurological strokes (ischemic or hemorrhagic strokes, post heart-lung by-pass) has not been found. In agreement with the literature, it is in terms of intra-post-operative blood loss, although in our population they have a negative and significant impact on the outcome, while the data still acquired today is that there is only one trend of greater need for blood transfusions, but without impact on survival, however patients aged ≥ 85 yrs have a higher probability of intraoperative blood transfusion (51% vs. 30%, p < 0.001). Conversely, among patients < 80 years of age, chronic anemia may significantly increase the risk of early death (HR, 2.03; 95% CI= 1.47, 2.80), but not of late death (OR: 1.21 , 95% CI= 0.88, 1.67), this does not happen in octogenarians and ultra-octogenarians (risk of early death HR, 1.47, 95% CI = 0.84, 2.56; risk of late death: HR, 0.92 95% CI = 0.50, 1.69) (14).

All the variables in can have an impact (i) on both the length of stay in intensive care and on the hospital stay (usually about 1.5 or 2 times greater than patients under 80 years of age) [5]; (ii) both on costs and above all on mortality. Cardiac surgery in octogenarians and ultra-octogenarians is correlated with a significantly higher 30-day mortality (3.1-21%, versus 1.6-2.2), but, it would seem, not with a prolonged stay in therapy intensive or higher costs [3,9,11,14,22,24-26], as also emerges in the present work. However, in general in cardiac surgery patients who, due to post-operative complications, require a prolonged stay in intensive care, mortality increases considerably and reaches a peak in the range: 31-56.5%) [4] and likewise increases - as in our case – the risk of acquiring VAP.

Encephalic and Vascular complications in octogenarians had an acceptable perioperative risk and long-term outcome. Considering high risk of 2-year MACCE, intervention strategy should be more cautious for patients with carotid artery disease. Octogenarians with arrhythmia and CHF should receive stricter postoperative management in case of MACCE [25].

Furthermore, compared to the literature data which report long-term mortality, it is higher in combined CABG + AVR interventions than in CABG alone (4.3% vs 5.4%, respectively, although not significantly) [22]. The literature shows that 30-day mortality is substantially different stratifying by type of operation: 8.8% in CABG, 12.8% in single-valve and 18.9% in combined operations (valve replacement and CABG). After 5 years of follow-up, survival did not differ between types of intervention (p = 0.62) [23]. Surgical interventions for acute type II aortic dissection should be considered as a prospect for octogenarians and ultra-octogenarians, given the good long-term quality of life recorded [27]. Among other things, octogenarians and ultra-octogenarians, compared to under 80, seem to have a lower probability (i) of developing mal-perfusion (9% vs 40%, p = 0.002); (ii) undergoing a Bentall-type surgery (5% vs 24%, p = 0.04); (iii) having long times of circulatory arrest (16 ± 9 minutes vs. 20 ± 7 minutes, p = 0.03); (iv) lower in-hospital mortality [26] early and late (early and late death), although intra-operative mortality is still significantly higher than in younger patients (40% vs 18%, p = 0.04) [16].

Furthermore, in our series, short-term mortality did not differ significantly between the different types of surgery [coronary artery bypass graft (CABG): 5.1%, valve replacement: 7.6%, p = 0.51) [8]. Even among patients over octogenarians, hospital survival is similar, once stratified by type of intervention (coronary or valvular) [8,19].

Mortality is higher in combined CABG + AVR interventions than in CABG alone (4.3% vs 5.4%, respectively, although not significantly) [27]. We preferred to include the type of pathology (valvular, coronary, combined and aortic) in the predictive model rather than the type of intervention. This is because the diversity of pathologies is certainly more likely to have an impact on the outcome - understood as "early death", than a mechanistic and in fact reproducible act on itself such as surgery, especially in a routine regime. Moreover, in our population, aortic surgery seems to be significantly involved in the "early death" condition, above all because it is surgery of greater weight and often of urgency/emergency. Conversely, the present study shows a different survival according to the type of intervention and between age groups. The 30-day mortality was substantially different when stratified by type of intervention, 8.8% in CABG, 12.8% in single-valve and 18.9% in combined interventions (valve replacement and CABG).

Concordance is also evident between the predictor scores of intra-operative cardio-anesthesiological risk as described by Di Eusanio et al. The main predictors of outcome in patients (O) and (>O) detectable in the literature are the following: (i) NYHA III-IV (OR = 2.7, 95% CI = 1.2-6 .7) and CCS III-IV (OR = 3.1, 95% CI = 1.1-9.4) [11]. Different behavior is recorded for the redo/recurrence variable, which for our series is not important while the literature indicates that a previous cardiac surgery is correlated with a greater risk of early death: (HR = 2.23, 95% CI = 1.23-4.64, p = 0.007).

While for the international literature the previous heart surgery: (HR = 2.23, 95%CI=1.23-4.64, p = 0.007) is among the predictive factors of mortality together with: (i) NYHA III-IV (OR = 2.7, 95 %CI=1.2-6.7) and CCS III-IV (OR = 3.1, 95%CI=1.1-9.4) [11], (ii) age (HR = 1.25, 95%CI=1, 09-1.43, p = 0.001 for each extra); (iii); (iv) previous stroke (HR = 2.39, 95%CI=1.25-3.98, p = 0.01) (8.19); (iv) preoperative chronic renal failure (OR = 11.1, p <0.048) and postoperative acute renal failure (OR = 10.16, p <0.0001) [8]; (v) postoperative arrhythmias (OR = 3.44, p < 0.022); (vi) sepsis (OR = 37.38, p <0.0001), pneumonia (OR = 8.29, p <0.038) [29].

The present work agrees with those published in the sense that an impact of a greater duration of aortic clamping time and CEC time was found, trusting us on a greater predictive efficacy of two variables, compared to the dichotomized CEC, often collected in studies

Unfortunately, a significant limitation of our study is that we are unable to make comparisons of mortality 1, 3, 5 years after surgery, as well as with regard to neurological outcome. One of the strength of the study has been to find out pre-operative predictors of outcome, in a view to highlight of the pre-selection of the elderly undergoing heart surgery. Atladottir et al. performed a study population including 2342 patients age ≥80 years undergoing open-heart surgery. They observed an association between severely impaired preoperative renal function and death within 1-year postsurgery (odds ratio [OR], 4.6; 95% confidence interval [CI], 2.7-7.2). Furthermore, renal clearance <40 mL/min and prolonged cardiopulmonary bypass time of >180 minutes were associated with a >50% probability of death within 1 year. The adjusted OR for death within 1 year was increased significantly with a postoperative length of stay in intensive care of ≥3 days (OR, 5.9; 95% CI, 4.1-8.6) and a duration of postoperative mechanical ventilation ≥2 days (OR, 7.5; 95% CI, 4.1-13.9). Various preoperative and intraoperative characteristics were associated with in-hospital dialysis, in particular cardiopulmonary bypass time >180 minutes (OR, 11.6; 95% CI, 4.7-28.5) [30].

The intrinsic weakness of the model derives from the fact that the time of hospital stay was considered as the time of failure (occurrence of post-operative death), i.e. the time of stay in post-operative intensive care added to the time of stay in heart surgery.

This follow-up period is in fact too short and only allows us to think in terms of – de facto – "early" mortality, bearing in mind that a follow-up of 28 days or 3 months or 6 months would have made it possible to better interpret the main predictors of outcome, especially in terms of their impact on late mortality. Another bias is constituted by the absence - as a given - of the pre-intervention hospitalization, undoubtedly indicative of the severity of the heart disease, both coronary and valvular. On the other hand, to compensate for this "missing data", the model considered the scores for identifying the peri-operative anesthetic risk (CCS/CRS), as well as the chronic and acute comorbidities of the patients, in particular the pre-operative performance status of the cardiac pump, identifiable in the cardiogenic shock variable.

A weakness of the study we conducted is that there was no possibility - given the retrospective nature of the same - to analyze and compare data with less invasive methods.

One of the alternative options to surgical revascularization appears to be the percutaneous route (PCI) in the angiography room by the interventional cardiologist. In this regard: in the over 80s, 30-day mortality is 8.8% after CABG and 7.4% after PCI (p = 0.514). Evidence from the literature indicates an association between CABG and a significantly increased risk of 30-day mortality (OR: 2.246, 95%CI=1 under 80.141-4.422) in octogenarians, although - patients undergoing PCI and CABG - showed survival similar, after adjustment for propensity score matching (66.4% CABG vs 58.9% PCI, p = 0.730) [18]. At 30 days postoperatively, a major or adverse cardiac or cerebral event (MACCE) may occur in octogenarians and over octogenarians, in approximately 11.4% in the PCI group vs. 44.4% in the CABG group (p < 0.001); results in an overall mortality of 2.5% in the PCI group vs. 8.3% in the CABG group (p = 0.05); and a mortality from cardiovascular causes of 1% vs. 5% (p = 0.046); a mortality from sepsis 1.5% vs 1.5% (p = 1.0) not different from; a recurrence of acute myocardial infarction 5.4% vs. 4.8% (p = 0.74). The need for new revascularization at 30 days is evident in both techniques [18]. Furthermore, at 24 months of follow-up the MACE was 35.2% in the PCI group vs 27.9% in the CABG group (p = 0.36); overall mortality (11.3% vs. 27.9% p = 0.002) in patients over 80 undergoing PCI compared to those undergoing CABG is different from that for cardiovascular causes (1.5% vs 11.5% (p <0.001). However: (i) the need for repeat cardiac revascularization was higher in the PCI group (20.3% vs 0%, p < 0.001); (ii) hospital stay was higher in the CABG group (4.7 +/- 9 vs. 16.8 + / - 17.4 days, p = 0.01) [27]. However, these data do not allow directing - if not individualizing it - daily practice towards one of the two specific revascularization techniques.

Several studies confirm that off-pump CABG surgery (OCABG) remains a valid option for myocardial revascularization, being able to optimize the outcome in elderly patients. From the meta-analysis of 14 studies in the literature on 4,991 patients >80 years, of whom 3,113 underwent conventional CABG (62.4%), and 1,878 (37.6%) underwent off-pump CABG, it emerged that mortality, stroke occurrence and post-operative respiratory failure were significantly higher in the conventional extracorporeal circulation group. Furthermore, a lower occurrence of postoperative stroke was observed (0%, 95%CI=0-0 vs 3.6%, 95%CI=0-10.0, P = 0.50) after OPCAB [20,29] five-year survival was 81.0% after OPCAB and 78.1% after CCAB (p = 0.239). An additional analysis of only eight studies (3416 patients), showed a significantly higher risk of postoperative stroke after conventional CABG (4.2%, 95%CI=2.4-7.1 vs. 1.5%, 95%CI=0.9-2.5, hazard ratio (RR) 2.15, 95%CI=1.17-3.96, p = 0.01). A second systematic review highlighted: a higher immediate postoperative mortality after conventional CABG following a meta-analysis involving 15 studies, 4409 patients: this mortality was equal to 6.5%, 95%CI=5.2-8.0 vs. 5.6%, 95%CI=4.2-7.4, RR = 1.29, 95%CI=0.86-1.93, P = 0.21). Recent studies indicate that OPCAB versus CCAB in octogenarians and ultra-octogenarians is associated with a significantly lower postoperative stroke risk and improved early survival (33). Again, however, the evidence does not allow to direct daily practice towards one of the two specific revascularization techniques.

Volk et al. performed a study by which showed About 397,713 patients were identified including 86,345 (21.7%) aged 80 and above. Octogenarians had higher in-hospital mortality for all procedures: CABG (4.94% vs. 2.39%, p < .001), VHS (5.49% vs. 4.08%, p < .001), and CABG + VHS (7.59% vs. 5.95%, p < .001), and this relationship persisted when gender, race, comorbidities, and type of hospital admission were controlled for: CABG (odds ratio [OR] = 1.71; 95% confidence interval [CI] 1.62-1.81); VHS (OR = 1.18; 95% CI 1.11-1.27); and CABH + VHS (OR = 1.17; 95%CI 1.10-1.26). Female gender, renal, or heart failure, nonelective admission, and CABG + VHS were associated with increased risk of in-hospital mortality. Octogenarians had higher rates of these factors (p < .001). The effect size of renal and heart failure and type of surgery was smaller for octogenarians [34].

The trans-catheter AVR technique (TAVI) was developed in order to minimize operative stress and trauma in high-risk patients, such as octogenarians and ultra-octogenarians and has likely become the standard for the elderly ©Indeed preoperative frailty reduced the rate of discharge to home of such patients [35,36]. Patient selection for TAVI is still a matter of debate and octogenarians and octogenarians over are often regarded as high-risk patients. Moreover, patients undergoing TAVI usually have more comorbidities: pre-existing renal insufficiency/dysfunction (31% vs. 56%, p = 0.001); peripheral vascular disease (6% vs. 30%, p < 0.001); diabetes mellitus: (19% vs 49%, p <0.001); reduced ejection fraction (LVEF <30%: 2% vs. 13%, p <0.05); pulmonary hypertension (23% vs 48%, p < 0.005); an increase in perioperative risk represented by Euro-SCORE (conventional AVR: 11% ± 1.27 vs. TAVI 38% ± 1.35, p <0.0005). Furthermore, the 30-day all-cause mortality was found to be 5.6% in the AVR cohort and 8.8% in the TAVI cohort (p = 0.55, while the cardiovascular mortality was 3.4% and 7.6% (p = 0.03) The same investigation revealed actuarial survival at 6 months and 1 and 2 years of 89.8% and 74%, respectively in AVR and TAVI patients of 85% at six months [20].

Unfortunately another weakness of our study is the very short time follow-up of the patients after discharging form hospital. Indeed Aksit et al. studied a total of 245 patients aged 80-93 years were evaluated in the study. The patients were followed up 5.4±3.7 years after open-heart surgery. In-hospital mortality rates were 10% in elective cases and 15.1% overall. Age ≥85 years, chronic kidney disease, chronic obstructive pulmonary disease, and emergency surgery were independent predictors of in-hospital mortality. The median survival time was found to be 4.4±0.3 years for all participants. The long-term survival of patients who underwent emergency cardiac surgery was significantly lower than that of elective patients (log-rank <0.001) [37].

It was difficult for us to evaluate the rehabilitation aspect which certainly constitutes a bias. Octogenarian and ultra-octogenarian patients who are never able to be discharged home, even after the rehabilitation cycle following discharge from the heart surgery center, have a lower medium-long-term survival, compared to under 80s (85.8% vs 94.6 %, p = 0.009; 80.1% vs 90.3%, respectively, p = 0.01) [38]. In octogenarian and ultra-octogenarian patients with reduced ejection fraction, both coronary and valvular interventions appear to be correlated with a substantially acceptable short-term mortality, as evidenced by recent literature (40% vs. 15 in patients <80 years) [39]. There is little evidence on quality of life after surgery [40,41], showing that four years after surgery, 95.2% of octogenarians live alone, with a partner or relatives, and only 4.0% require permanent assistance home nursing. Functional capacity emerged to be on average high, and with no significant difference between under and over 80s (< 80: 87 ± 22 and? 80: 67 ± 31, p = 0.108). Other studies report that among the survivors, most are self-employed (66%) and 8% dependent on relatives or institutionalized; seventy percent live at home, 19% in a residence, and 9% in a sheltered care facility. More than 90% of patients over 80 and survivors of cardiac surgery carry out leisure activities also in social sectors, with good cognitive and physical feedback [40,41]. Comparing the answers given to a questionnaire administered before surgery and after 12 months, 83% of patients showed an improvement in quality of life and only 4% presented a decline in cardiac functional performance [40,41].

Finally, referring to the two Cox models, elaborated by removing the categorical variable age ≥ 85 yrs. or < 85 yrs. a different behavior of the predictors of survival to hospital death is highlighted, which are reduced in number and electively pre-operative, in patients over 85 yrs. while increased and electively post-operative in the case of patients under 85 yrs. Moreover patients under 85 years old should have been stratified into 3 age groups: aged ≤ 50 years, with 50 < age ≤ 65 years and 65 < age ≤ 80 years. Unfortunately it should have been difficult or impossible to set a multivariate predictive model.

Moreover we do not stratified analysis according specific period of time since 1999 up to 2019. Indeed it is likely that the operative outcome is supposed to grow despite the increasing prevalence of comorbidities, because of improvement of surgical and anestesiologic techniques [41,42].

In conclusion our data suggest the importance of the age variable as well as the fact that the two populations are distinct and different. For this purpose and to reduce a bias effect linked both to age but above all to the difference in number between the two groups, a further and future multivariate analysis will be conducted with the use of propensity score matching.

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