

## CLINICAL SCIENCE

# PROGNOSTIC FACTORS FOR MORTALITY AMONG PATIENTS ABOVE THE 6<sup>TH</sup> DECADE UNDERGOING NON-CARDIAC SURGERY: (CARES – CLINICAL ASSESSMENT AND RESEARCH IN ELDERLY SURGICAL PATIENTS)

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**PURPOSE:** To ascertain perioperative morbimortality and identify prognostic factors for mortality among patients  $\geq 55$  years who undergo non-cardiac surgery.

**METHODS:** A retrospective cohort of 403 patients relating to perioperative morbidity-mortality. Data were collected from a standardized protocol on gender, age, comorbidities, medications used, smoking, alcohol abuse, chronic use of benzodiazepine, nutritional status, presence of anemia, activities of daily living, American Society of Anesthesiology classification, Detsky's modified cardiac risk index - American College of Physicians, renal function evaluation, pulmonary risk according to the Torrington scale, risk of thromboembolic events, presence of malignant disease and complementary examinations.

**RESULTS:** The mean age of the subjects was  $70.8 \pm 8.1$  years. The "very old" ( $\geq 80$  years) represented 14%. The mortality rate was 8.2%, and the complication rate was 15.8%. Multiple logistic regression showed that a history of coronary heart disease (OR: 3.75;  $p=0.02$ ) and/or valvular heart disease (OR: 31.79;  $p=0.006$ ) were predictors of mortality. The American Society of Anesthesiology classification was shown to be the best scale to mark risk (OR: 3.01;  $p=0.016$ ). Nutritional status was a protective factor, in which serum albumin increases of 1 mg/dl decreased risk by 63%.

**DISCUSSION:** The results indicate that serum albumin, coronary heart disease, valvular heart disease and the American Society of Anesthesiology classification could be prognostic predictors for aged patients in a perioperative setting. In this sample, provided that pulmonary, cardiac and thromboembolic risks were properly controlled, they did not constitute risk factors for mortality. Furthermore, continuous effort to learn more about the preoperative assessment of elderly patients could yield intervention possibilities and minimize morbimortality.

**KEYWORDS:** Surgery. Preoperative. Mortality. Risk. Evaluation.

## INTRODUCTION

In past several decades, it was commonly recommended that surgery for the elderly be avoided because of their frailty and increased risk when undergoing a major operative procedure. However, recent advances in anesthetic practice and surgical techniques, including minimally invasive surgical

approaches, have enabled sicker and older patients to be eligible for procedures that were more risky in the past.<sup>1</sup>

The perioperative care of elderly people is influenced by the particular alterations to aging, such as the presence of comorbidities, the use of multiple medications and the severity of the disease requiring intervention. Atypical presentations of diseases, diminished heart and lung reserves and alterations in the pharmacodynamics and pharmacokinetics of drugs are also observed.<sup>2,3</sup>

It must be kept in mind that much of the current management during the perioperative period for elderly patients is based on data from the non-elderly adult population. There

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is a need to define specific parameters for the elderly, and particularly for the very old.<sup>4</sup>

The concern now is that, because an increasing number of sicker and older patients are having surgery, perioperative morbidity and mortality rates may be increasing. As a result, there is a renewed interest in identifying factors associated with adverse postoperative outcomes to develop strategies to improve the perioperative care of and outcomes for geriatric surgical patients. Under these conditions, perioperative evaluation gives rise to the need for an comprehensive approach, with the objectives of minimizing risk as well as maintaining or recovering previous functional abilities.<sup>2</sup>

## Design

This retrospective cohort study investigated perioperative morbidity-mortality among elderly inpatients of Hospital das Clínicas between February and November 2004. The study was conducted by administering a structured preoperative evaluation and postoperative follow-up until the outcome of death or discharge.

## SAMPLE AND METHODS

Preoperative evaluations were performed on patients of both sexes aged 55 years and over. The exclusion criterion was failure to proceed with surgery.

After ethical approval, a single researcher reviewed the medical records made available by the Medical Archives Service and information present in the preoperative assessment file, with the objective of retrieving the clinical data.

The following data were collected from a standardized protocol: sex, age, comorbidities, medications used, smoking, alcohol abuse, chronic use of benzodiazepine, nutritional status, presence of anemia, activities of daily living (ADL), American Society of Anesthesiology (ASA) classification, Detsky's modified cardiac risk index – American College of Physicians (ACP), pulmonary risk according to the Torrington scale, risk of thromboembolic events, presence of malignant disease and complementary examinations (electrocardiogram, chest radiograph, hemogram, urea, creatinine, albumin, electrolytes and glycemia).

The primary outcome was the occurrence of in-hospital death.

After clinical evaluation and risk estimative, the CARES group (Clinical Assessment and Research in Elderly Surgical patients) applies guidelines focused on minimize risk including to start the beta blockade treatment to maintaining the heart rate below 70 beats per minute for high and intermediate cardiac risk, as suggest by the international recommendations.<sup>8-14</sup> Stress imaging testing like sestamibi SPECT

scan was indicated in selected cases.

The chronic renal failure stage  $\geq 3$  should carefully balancing fluids, avoid nephrotoxic drugs and use renal clearance to corrected antibiotic. These patients were seeing besides a nephrologist. The high respiratory risk was target to physiotherapy. We oriented non pharmacological preventive measures from thromboembolism for all patients and heparin therapy for high and intermediate risk. We accompanying all patients until discharge and complications were registered.

The variables relating to death ( $p < 0.10$ ) in the univariate analysis were grouped for applying logistic regression, and each of the groups was reduced by means of a stepwise selection process. Considering the variables thus selected, the backward stepwise method was applied to obtain the principal predictors of mortality. The Hosmer-Lemeshow test was used for adjustment of the end model.

For the statistical analysis, the MINITAB 14 program was used for descriptive analysis and comparison between patients with opposite outcomes. For continuous variables, Student's t-test or the non-parametric Kruskal-Wallis test were used. Qualitative variables were compared using the Pearson Chi-Square or Fisher's exact tests. Two-sided p-values  $< 0.05$  were considered significant.

## RESULTS

### Descriptive and univariate analysis

Among 508 patients enrolled, 105 (20.7%) fulfilled the exclusion criteria. Thus, 403 patients were studied.

The mean age was  $70.8 \pm 8.1$  years, with a range from 55 to 92 years. The very elderly ( $\geq 80$  years) represented 14% (Table 1). Elective surgery performs 88.9%, 67.2% cases were in the digestive system with malignant disease in 58% (Table 2).

**Table 1** - Clinical characteristics of cohort patients, according to the outcomes.

	SG (n=370)	DG (n=33)	p-value
Age (years) <sup>a</sup>	70.7 $\pm$ 8.1	72.3 $\pm$ 7.3	0.249
Male sex - n (%)	176 (48)	23 (70)	<u>0.017</u>
ADL dependence - n (%)	05 (02)	01 (11)	0.177
Malignancy - n (%)	206 (56)	28 (85)	<u><math>\leq 0.001</math></u>

SG – survivor group; DG – death group; ADL – activities of daily living;

<sup>a</sup> M  $\pm$  SD -mean  $\pm$  standard deviation.

Women predominated (51%), but there were more deaths among men ( $p = 0.017$ ; OR: 2.26; 95% CI: 1.08 – 4.72). Regardless of age, the number of comorbidities, the presence

**Table 2** – Surgical types evaluated

Type of Surgery	n	%
Digestive system elective	271	67.2
Emergency surgery	44	10.9
Gynecological	38	9.4
Urological	11	2.7
Vascular	10	2.5
Ear, nose and throat	10	2.5
Head and neck	07	1.7
Plastic surgery	07	1.7
Ophthalmological	05	1.2

of malignant disease as a surgical diagnosis and ASA and Detsky surgical risk classifications presented similar distributions between the sexes.

The comorbidities are listed in table 3. The number of diseases ( $3.9 \pm 1.7$ ) or the number of medications used ( $2.6 \pm 1.8$ ) per patient did not correlate with death. When specific diseases were evaluated, we was found that dyslipidemia, chronic kidney disease, valve disease (aortic or mitral), anemia, and history of coronary artery disease contributed towards increased surgical risk. The use of benzodiazepine longer than three months (4.7%), alcoholism (4.7%) and current smoking (11.9%) or stop smoking longer than three

**Table 3** – Cohort patients: comorbidities, according to the outcomes

Comorbidities	SG n(%)	DG n(%)	<i>p-value</i>
Hypertension	213 (58)	24 (73)	0.09
Anemia	100 (27)	17 (52)	<u>0.004</u>
Diabetes mellitus	76 (21)	7 (21)	0.93
Dyslipidemia	39 (11)	8 (24)	<u>0.04</u>
Coronary disease	21 (06)	8 (24)	<u>&lt;0.001</u>
Cardiac failure	25 (07)	3 (09)	0.47
Hypothyroidism	27 (07)	0 (00)	0.15
COPD <sup>a</sup>	24 (06)	1 (03)	0.70
Stroke	19 (05)	3 (09)	0.40
Atrial fibrillation	17 (05)	4 (12)	0.08
Chronic kidney disease stage $\geq 3$	11 (03)	7 (21)	<u>&lt;0.001</u>
Depression	13 (04)	2 (06)	0.35
Body mass index $<16$	6 (02)	5 (16)	<u>&lt;0.001</u>
Dementia	6 (02)	2 (06)	0.13
Heart valve disease	1 (0.3)	3 (09)	<u>&lt;0.001</u>

SG - survivor group; DG - death group; <sup>a</sup>chronic obstructive pulmonary disease.

months (28.3%) did not increase the mortality related to the operation.

The nutritional profile (Table 4) was seen to be a good prognostic factor, given that the mean hemoglobin, albumin and body mass index were lower among the patients who died, and these patients presented means that were below the reference values normally used.

**Table 4** – Evolution related to nutritional assessment in the cohort

	Reference values	SG (n=370) M $\pm$ SD <sup>a</sup>	DG (n=33) M $\pm$ SD <sup>a</sup>	<i>p-value</i>
Body mass index – kg/m <sup>2</sup>	20–25	24.6 $\pm$ 5.3	21.3 $\pm$ 5.0	<u>0.011</u>
Hemoglobin – g/dL	12–18	12.5 $\pm$ 2.2	11.2 $\pm$ 2.1	<u>0.002</u>
Albumin – g/dL	3.5–5.0	3.7 $\pm$ 0.7	2.9 $\pm$ 0.9	<u>&lt;0.001</u>
Lymphocytes – 10 <sup>3</sup> cell/mm <sup>3</sup>	1.0–3.4	1.7 $\pm$ 0.7	1.4 $\pm$ 0.7	0.084

SG - survivor group; DG - death group; M  $\pm$  SD <sup>a</sup> -mean  $\pm$  standard deviation.

General surgical risk, as classified by the ASA (Table 5), was shown to be progressively greater in accordance with the ASA grading, and it was correlated with mortality.

**Table 5** – Evolution related to ASA classification

ASA	SG n(%)	DG n(%)
I	56 (15)	00 (00)
II	292 (79)	27 (82)
III	22 (06)	05 (15)
IV	00 (00)	01 (03)
Chi-squared for trend <i>p</i> = 0.001		

SG – survivor group; DG – death group; ASA – American Society of Anesthesiology.

For Detsky's modified cardiac risk index, 208 (52%) patients were classified as low risk, 193 (48%) as intermediate risk and 2 (0.5%) as high risk. The mortality rate was 7.2% for the low-risk category, 8.8% for those at intermediate risk and 50.0% for those at high risk, which did not represent any significant difference.

The pulmonary and renal risks were low for most of the patients, however the risk of thromboembolism was almost high (73%). The risk of thromboembolic events and the high renal risk correlated with death, in despite of what was found for pulmonary risk (Table 6).

This sample presented a mortality rate of 8.2% and

**Table 6** – Evolution related to the renal, thromboembolism and pulmonary risk

Risk	Low n(%)	Moderate n(%)	High n(%)
Renal risk; p=0.02			
SG (n=370)	304 (82)	39 (11)	27 (07)
DG (n=033)	23 (70)	03 (09)	07 (21)
Thromboembolism risk; p<0.001			
SG (n=370)	03 (01)	105 (28)	262 (71)
DG (n=033)	00 (00)	02 (06)	31 (94)
Pulmonary risk; p=0.20			
SG (n=370)	298 (80)	69 (19)	03 (01)
DG (n=033)	23 (70)	10 (30)	00 (00)

SG – survivor group, DG – death group.

a non-fatal complications rate of 15.8% (Table 6). In particular, cardiac (6%), renal (5%), pulmonary (7%), operative (wound dehiscence, hemorrhage, fistula, etc; 8%) and infectious (14%) complications contributed to greater mortality (Table 7).

### Multivariate analysis

Multivariate analysis via multiple logistic regression (Figure 1) indicated the variables that were prognostic for mortality. The presence of coronary disease (odds ratio: 3.75; p=0.02) almost quadrupled the risk of death, while heart valve disease (odds ratio, 31.79; p=0.006) increased the risk 31-fold.

Nutritional status was shown to be a protective marker: a serum albumin increase of 1 mg/dl decreased the risk of mortality by 63%.

**Table 7** – Complications of cohort patients, according to the outcomes

Complication	SG n(%)	DG n(%)	p-value
Infectious	31 (8)	25 (76)	<0.001
Surgical	21 (6)	11 (33)	<0.001
Pulmonary	16 (4)	13 (39)	<0.001
Cardiac	16 (4)	9 (27)	<0.001
Renal	5 (1)	15 (45)	<0.001
Electrolytic disorders	12 (3)	2 (6)	0.320
Delirium	10 (3)	3 (9)	0.081
Venous thromboembolic	2 (0.5)	1 (3)	0.226
Anesthetic	2 (0.5)	0 (0)	1.000

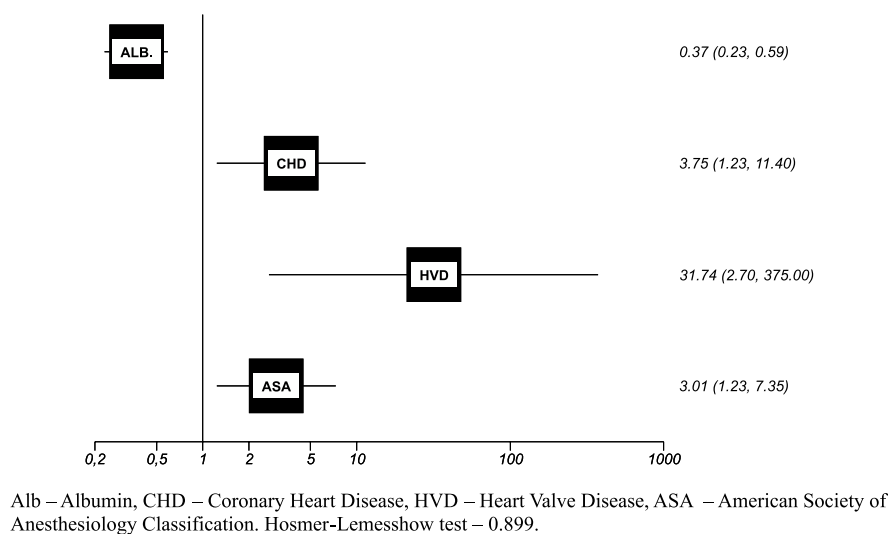
SG – survivor group; DG – death group.

ASA classification was shown to be better for estimating prognoses than the other risk scales used. On this scale, a one-unit increase tripled the chance of death.

The Hosmer-Lemeshow test (0.899) showed a good fit, 99.3% sensitivity, 25.0% specificity and 91.3% accuracy in retesting this model on the same sample.

### DISCUSSION

The limitations of this study are related to its retrospective design, which favors under-diagnosing of complications. For instance, the low incidence of delirium (3%) found in this population can be cited. It is known that hypoactive delirium is a condition that is frequently under-diagnosed by health teams and its impact on mortality often ignored.<sup>5,6</sup> Nevertheless, the deaths inside the hospital (primary outcome) were faithfully recorded by the institution. Standardization of the preoperative



**Figure 1** – Odds of death related to the prognostic factors on perioperative period

assessment file and the risk scales used gave uniformity to the data and made it easier to collect.

We worked with the bias that the majority of our patients underwent digestive system surgery. Incorporation of other surgical groups, such as those who underwent orthopedic surgery, urological surgery or neurosurgery, might have furnished different perspectives from that observed. Our population presented a high mean age and a high rate of comorbidities but a good functional capacity. Only 2% of our patients were dependent for Activities of Daily Living. Some comorbidities are related to worse perioperative prognosis as coronary artery disease and nowadays, there are many purposes to minimize this risk and the elderly is a population that potentially has beneficial effects of such interventions.<sup>8-14</sup>

Among the factors included in the multivariate analysis, the presence of mitral or aortic valve disease can be highlighted. The presence of symptomatic valve disease increases the surgical risk and involves a complex treatment that postpones possible non-cardiac surgery. Goldman's scale contraindicates surgery in patients with severe aortic valve disease, and the management of such patients currently raises interesting controversies.<sup>15-20</sup>

A poor nutritional profile is a known risk factor for infectious complications and wound dehiscence, thereby contributing towards greater perioperative mortality. Nutritional support benefits patients with severe malnutrition in perioperative period.<sup>21-26</sup> In the present study, there was greater correlation between mortality and the body mass index, albumin and hemoglobin. Albumin was highlighted in the logistic regression, in that an increase of 1 g/dl decreased the chance of death by 63%.

Regarding to the scales used for preoperatively evaluating the risks, there was a clear correlation between the ASA classification and mortality. It scores age and degree of clinical impairment by chronic diseases, where brief interventions generally produce disappointing results. A veterans' study<sup>7</sup> also saw the ASA classification as a precise predictor of mortality.<sup>21-26</sup>

The univariate association between thromboembolic risk and death reflects the particular criteria that scores high-risk (malignant disease, immobilization, cardiac insufficiency,

prolonged surgery, etc.). The majority (73%) of this study population was at high risk, but because of the wide use of adequate prophylaxis, only three occurrences of this complication were confirmed (0.7%). In other words, the real occurrences of venous thromboembolism were unrelated to greater mortality. In the literature, it is predicted that deep vein thrombosis will occur at a rate of 10 to 20%, and symptomatic pulmonary thromboembolism will occur at a rate of 5 to 10% in the absence of prophylaxis.<sup>27</sup>

The modified Detsky index showed similar mortality between low and intermediate risk. This was probably due to the advent of the use of beta-blockers, which may significantly diminish the risk of perioperative cardiac events in patients at intermediate risk. Our group systematically indicates the use of beta-blockers for patients at intermediate and high cardiac risk and suggests that this medication should be maintained for patients who are already using it at home as suggest by the literature.<sup>8-14</sup>

Pulmonary risk based upon the Torrington scale was not a predictor of mortality. This is in line with the literature and the guidelines of the American College of Physicians (2006), in which pulmonary risk does not contraindicate surgery. We recommend clinical control and respiratory physiotherapy as indicated for patients at risk.<sup>4,27,28</sup>

We conclude that, provided pulmonary and cardiac conditions and the risk of thromboembolism are properly controlled, they do not constitute risk factors for mortality. Therefore, surgical procedures on elderly people with such conditions should not be contraindicated. Instead, risk should be managed with a preventive attitude. The impact that these clinical interventions produce on mortality predictors reinforces the need for a comprehensive approach towards the elderly.

The results indicate that serum albumin, coronary heart disease, valvular heart disease and ASA classification could be prognostic predictors for aged patients in a perioperative setting. Furthermore, continuous efforts to learn more about the preoperative assessment of elderly patients could yield intervention possibilities and minimize morbimortality. More consistent data will come from prospective studies that are now in progress at our center.

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