Revista da Sociedade Portuguesa de Anestesiologia
http://revistas.rcaap.pt/anestesiologia
https://dx.doi.org/10.25751/rspa.24526

ARTIGO ORIGINAL

Are Frail Patients More Susceptible to Intraoperative Hypotension and 30-Day Mortality?

São os Doentes Frágeis Mais Suscetíveis a Hipotensão Intraoperatória e Mortalidade nos 30 Dias Pós-Operatórios?

Diana Fonseca[2,*], Fátima Gomes[1], Marisa Barros[2], Ana Rouxinol-Dias[1,3], Mariana Fernandes[2], Andreia Machado[2], Diana Rodrigues[2], João Lusquinhos[2], Flávia Oliveira[2], Daniel Rodrigues[2], Ana Silva[2], Joselina Barbosa[1], Fernando Abelha[1,2], Joana Mourão[1,2]

Afiliações
[1] Faculty of Medicine of University of Porto, Porto, Portugal.
[2] University Hospital Center of São João, Porto, Portugal.
[3] Center for Research in Health Technologies and Information Systems (CINTESIS), Faculty of Medicine, University of Porto, Porto, Portugal.

Keywords
Frailty; Hypotension; Intraoperative Complications; Postoperative Complications/mortality
Palavras-chave
Fragilidade; Hipotensão; Complicações Intraoperatória; Complicações Pós-Operatórias/mortalidade

ABSTRACT

Introduction: Frailty has been considered to be an important predictor of surgical morbidity, influencing both short and long-term postoperative mortality. Despite this association, less is known about frailty's impact on intraoperative hemodynamic stability, namely intraoperative hypotension, which may influence postoperative outcomes. We aimed to evaluate if frail patients submitted to elective surgery are more susceptible to experience intraoperative hypotension and mortality at 30 days.

Methods: A prospective cohort study was conducted between March and November 2020. Fifty-three adult patients proposed for intermediate or high-risk surgery were enrolled. Frailty was assessed preoperatively by Clinical Frailty Scale. Intraoperative hypotension, defined by three different criteria, and mortality at 30 days were evaluated for each patient.

Results: Of the 53 participants enrolled, 13.7% (n=7) were deemed frail. All frail patients developed intraoperative hypotension by at least one of the criteria in contrast with 82.9% (n=29) of non-frail, although differences were not statistically significant (p=0.567). Intraoperative hypotension cumulative duration did not differ significantly between groups in generalized linear model. The 30-day survival rate was 96.2% and frailty had a significant influence on overall survival (p=<0.001).

Conclusion: This study did not show an association between frailty and intraoperative hypotension development or it's cumulative duration. Though, it demonstrated that frailty, evaluated by Clinical Frailty Scale, is associated with decreased survival at 30 days postoperatively, which supports the routine use of this tool and outlights the importance of preoperative frailty screening.

RESUMO

Introdução: A fragilidade tem sido considerada um importante preditor da morbilidade cirúrgica, influenciando a mortalidade pós-operatória a curto e longo prazo. Apesar desta associação, pouco se sabe sobre o seu impacto na estabilidade hemodinâmica intraoperatória, nomeadamente hipotensão intraoperatória, a qual pode influenciar os resultados pós-operatórios. O nosso objetivo foi avaliar se pacientes frágeis, submetidos a cirurgia eletiva, são mais suscetíveis ao desenvolvimento de hipotensão intraoperatória e mortalidade aos 30 dias.

Métodos: Um estudo de coorte prospetivo foi efetuado entre março e novembro de 2020. Cinquenta e três adultos propostos para cirurgia de risco intermédio ou alto foram incluídos. A fragilidade foi aferida pré-operatoriamente pela Clinical Frailty Scale. A hipotensão intraoperatória, definida por três critérios diferentes, e a mortalidade aos 30 dias foram avaliadas para cada paciente.

Resultados: Dos 53 participantes incluídos, 13,7% (n=7) eram frágeis. Todos os pacientes frágeis desenvolveram hipotensão intraoperatória, definida por pelo menos um critério, em comparação com 82,9% (n=29) dos não frágeis, embora as diferenças não tenham sido estatisticamente significativas (p=0,567). A duração cumulativa da hipotensão intraoperatória não diferiu significativamente entre os grupos no modelo linear generalizado. A sobrevida aos 30 dias foi 96,2% e a fragilidade teve influência significativa na sobrevida global (p=<0,001).

Autor Correspondente/Corresponding Author*:
Diana Fonseca
Morada: Centro Hospitalar e Universitário de São João, Alameda Prof. Hernâni Monteiro, 4200-319 Porto, Portugal.
E-mail: print.dianaj@gmail.com

Conclusão: Este estudo não evidenciou associação entre fragilidade e o desenvolvimento ou duração cumulativa de hipotensão intraoperatória. Porém, demonstrou que a fragilidade, avaliada pela *Clinical Frailty Scale*, se associa a diminuição da sobrevida aos 30 dias, corroborando o uso rotineiro desta ferramenta e destacando a importância da avaliação pré-operatória da fragilidade.

INTRODUCTION

Frailty is considered a biological syndrome of decreased physiological reserve that leads to a greater vulnerability to adverse events and limits the overall capacity of a person to respond to stressors.[1-3]

The first definition of frailty was of Fried's physical phenotype, which considers that at least three of the following physical criteria should be met to diagnose frailty[2]: slow gait, low grip strength, weight loss, self-reported exhaustion, and low physical activity. Currently, there are many clinical tools to evaluate frailty based on physical performance, mobility, nutritional status, mental health and cognition, but there is still no consensus on the best clinical tool to assess frailty.[2,3]

An increasing interest has emerged in preoperative frailty assessment since many studies pointed frailty as an important predictor of surgical morbidity and mortality.[4-7] Indeed, frailty has shown a strong association with postoperative short-term (30-day) and long-term (1-year) mortality across different surgical subspecialties.[8,9] Furthermore, although this relationship is typically described in older people, frailty has also demonstrated to be a potential indicator of the risk of death in non-elderly individuals.[8]

Despite the well-established association between frailty and poor postoperative outcomes,[6,7] less is known about the influence of frailty during the intraoperative period, namely in patient hemodynamic stability, which may influence postoperative outcomes.

The relationship between frailty and intraoperative hypotension (IOH) is not well studied but frailty seems to be associated with cardiac autonomic nervous system impairment. In fact, frail patients suffer a progressive homeostatic deregulation in many physiological systems, including autonomic nervous system which manifests itself in heart rate variability reduction or decreased heart rate response to physical activity.[10] This cardiovascular autonomic dysfunction can contribute to blood pressure instability that may occur during surgery.[11]

Additionally, there is evidence that intraoperative hemodynamic instability, namely IOH, can be associated with inadequate organ perfusion and risk of organ injury. The latter seems to increase with progressive decreases in blood pressures and prolonged exposition to low blood pressures, although there is not a consensus threshold to define IOH.[12,13] These findings corroborate reports showing that, similarly to frailty, IOH increases postoperative morbidity and mortality.[14,15]

We conducted a prospective cohort study with the aim of evaluating if frail patients submitted to elective intermediate or high-risk surgery are more susceptible to experience IOH and have greater risk of mortality at 30 days.

MATERIAL AND METHODS

STUDY DESIGN

We performed a prospective cohort study in a university hospital between March and November 2020. It should be noted that, due to concerns with coronavirus disease 2019 (COVID-19) dissemination, declared pandemic by the World Health Organization (WHO) on March 11, elective surgical activity and data collection process for this study were suspended for a large period of time.

The study was approved by the Hospital Ethics committee and informed written consent was given by all the patients.

PARTICIPANTS

Inclusion criteria were defined as adult patients proposed for intermediate or high-risk surgery (according to ESC/ESA Guidelines on non-cardiac surgery)[16] under general, regional or combined anesthesia, of Portuguese nationality. Patients proposed for low-risk surgery, cardiac or intracranial surgery, urgent/emergent surgery, with admission to Intensive Care Unit (ICU), with inability to understand Portuguese language and to understand or sign a written informed consent were excluded.

Fifty-three patients admitted to surgery met inclusion criteria to the study and were enrolled. Data collected in the preoperative period included: surgical risk (stratified by American Heart Association guideline); patient sociodemographic data; comorbidities by American Society of Anesthesiologists (ASA) physical status classification and Charlson Comorbidity Index (CCI)[17]; Revised Cardiac Risk Index (RCRI)[18]; usual medication, particularly antihypertensive drugs, highlighting angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor blockers and beta-adrenoreceptor blockers. Polypharmacy was defined by the use of ≥ 5 drugs. Patient frailty was assessed by the Clinical Frailty Scale (CFS) and patients were considered frail when the score was superior or equal to 5, whereas a patient with a score inferior to 5 was considered non-frail.[19]

Intraoperative data, collected from anesthesia records, included blood pressure monitoring data, inotropes/vasopressors use and length of surgery. Blood pressure measurements were obtained either by an automatic noninvasive blood pressure cuff every 3-5 minutes or continuously by an indwelling arterial line. In the cases where both measures of blood pressure were available, the

data from the arterial line was used. Posteriorly, anesthesia records were analysed to assess for IOH.

Hypotension was classified by three criteria: A- Mean arterial pressure (MAP) less than 65 mmHg for longer or equal to 15 min; B1- Systolic blood pressure (SBP) less than 90 mmHg; B2 - SBP between 90 and 99 mmHg.

The cumulative duration (in minutes) of IOH periods was recorded as the sum of every IOH episode duration according to criteria A, B1 and B2. The lowest systolic blood pressure observed and the need of inotropes or vasopressors in the intraoperative period in order to treat hypotension was also registered. Blood pressures were considered out-of-range according to the following criteria: SBP greater than or equal to 300 or SBP less than or equal to 20 mmHg; SBP less than or equal to DBP + 5 mmHg; DBP less than or equal to 5 mmHg or DBP greater than or equal to 225 mmHg.

In the postoperative period, clinical records of all participants enrolled in the study were evaluated to assess mortality within the period of 30 days after surgery.

STATISTICAL ANALYSIS

A descriptive statistics of all variables collected was performed. In case of qualitative variables, absolute (n) and relative frequencies (%) were calculated. For quantitative variables, all used variables follow a non-normally distribution according to Kolmogorov-Smirnov and Shapiro-Wilk tests and median and [interquartile range (IQR)] were determined. Fisher's exact test was used to describe the association between categorical variables and Mann-Whitney U test was used to assess ordinal and continuous variables.

Logistic regression analysis was performed to assess the relationship between frailty and the use of vasopressors, with adjustment for potential confounders (age and sex). A generalized linear model, also adjusted for age and sex, was calculated to compare the cumulative duration of IOH between frail and non-frail participants.

Survival rate at 30-day was calculated using a Kaplan-Meier estimate and the log-rank test was performed to compare survival curves.

A p-value<0.05 was considered statistically significant. Statistical analysis of the collected data was done with Statistical Package for Social Sciences (SPSS) software, Chicago, Illinois, v26.0.

RESULTS

PREOPERATIVE DATA

Fifty-three patients were enrolled in the study. However, due to computer technical problems, intraoperative arterial tension records were not accessible in 10 participants and this was considered missing data. The median [IQR] age of participants was 61 [54.5-69.5] years, being mainly female (54.7%). Demographic characteristics of this cohort are presented in Table 1. Using Clinical Frailty Scale, 7 (13.7%, 2 missing value) participants were classified as being frail (CFS 5-9) and the remaining 44 (86.3%, 2 missing value) as non-frail (CFS 1-4). Main characteristics of both groups (frail and non-frail participants) are described in Table 2.

Table 1. Demographic characteristics of participants

Characteristic	Participants N=53 (%)
Age, median, [IQR], y	61.5 [54.5-69.5]
Gender	
Female	29 (54.7)
Male	24 (45.3)
ASA class	
I	2 (3.8)
II	28 (52.8)
III	22 (41.5)
IV	1 (1.9)
V	0 (0.0)
VI	0 (0.0)
Frailty	
1 (Very fit)	2 (3.8)
2 (Fit)	14 (26.4)
3 (Managing well)	20 (37.7)
4 (Living with very mild frailty)	8 (15.1)
5 (Living with mild frailty)	2 (3.8)
6 (Living with moderate frailty)	2 (3.8)
7 (Living with severe frailty)	3 (5.7)
8 (Living with very severe frailty)	0 (0.0)
9 (Terminally ill)	0 (0.0)
Missing	2 (3.8)
Charlson Comorbidity Index	
0	7 (13.2)
1	5 (9.4)
2	11 (20.8)
3	3 (5.7)
4	6 (11.3)
5	5 (9.4)
6	2 (3.8)
7	1 (1.9)
8	2 (3.8)
9	1 (1.9)
10	1 (1.9)
Missing	9 (17.0)
RCRI	
0 points	13 (24.5)
1 points	30 (56.6)
2 points	6 (11.3)
3 points	2 (3.8)
4 points	1 (1.9)
5 points	0 (0.0)
6 points	0 (0.0)
Missing	1 (1.9)
Polypharmacy	
Yes	20 (37.7)
No	33 (62.3)
Antihypertensive drugs	
No	29 (54.7)
ACE inhibitor	10 (18.9)
Angiotensin II receptor blocker	7 (13.2)
Others	7 (13.2)
Surgical Risk	
Intermediate	42 (79.2)
High	11 (20.8)

Legend:
IQR Interquartile Range; ASA American Society of Anesthesiology classification; RCRI Revised Cardiac Risk Index

Table 2. Demographic characteristics of frail and non-frail participants

	Frail Participants (N=7, 13.7%)[a]	Non-frail Participants (N=44, 86.3%)[a]	*p* value[b]
Age, median, [IQR], y	73 [60-82]	60 [53-67]	0.022
Gender, n (%)			
Female Male	1 (14.3) 6 (85.7)	27 (61.4) 17 (38.6)	0.037
ASA			
I II III IV	0 (0.0) 3 (42.9) 3 (42.9) 1 (14.3)	2 (4.5) 24 (54.5) 18 (40.9) 0 (0.0)	0.218
CCI, median [IQR]	5 [2-6]	2 [1-4]	0.205
RCRI			
0 1 2 3 4	3 (42.9) 2 (28.6) 1 (14.3) 0 (0.0) 1 (14.3)	10 (23.3) 26 (60.5) 5 (11.6) 2 (4.7) 0 (0.0)	0.132
Polypharmacy	4 (57.1)	15 (34.1)	0.402
Antihypertensive drugs			
No ACE inhibitor ARB Others	4 (57.1) 1 (14.3) 0 (0.0) 2 (28.6)	25 (56.8) 8 (18.2) 6 (13.6) 5 (11.4)	0.616
Surgical Risk			
Intermediate High	6 (85.7) 1 (14.3)	34 (77.3) 10 (22.7)	1.000
Surgery length, median [IQR]	311 [139-542]	220 [162-335]	0.417

Legend:
[a] 2 missing values
[b] Categorical data comparison analysis was made using Fisher's exact test and continuous data comparison analysis was made using Mann-Whitney U test. P value for 2-sided significance.
IQR Interquartile Range; ASA American Society of Anesthesiology classification; CCI Charlson Comorbidity Index; RCRI Revised Cardiac Risk Index; ACE inhibitor Angiotensin-converting Enzyme inhibitor; ARB Angiotensin Receptor Blockers.

INTRAOPERATIVE DATA

IOH by at least one of the above-mentioned criteria was registered in a total of 37 participants (86.0%, 10 missing values). Criteria A, B1 and B2 was verified in 25.6%, 72.1% and 81.4% of the participants, respectively (Table 3).

Median [IQR] length of surgery was 220 [162-350] minutes. Of note, IOH was verified in 100% (n=9) of participants submitted to high-risk surgery and in 82.4% (n=28) of participants submitted to intermediate risk surgery. Median [IQR] minimal systolic blood pressure was 76 [65-91] mmHg. The drug most commonly used to treat hypotension was ephedrine (bolus).

Table 3. Intraoperative hypotension defined by Criteria A, B1 and B2

	Participants meeting hypotension criteria[a] N (%)	Duration of hypotension[a] Median [Interquartile range], minutes	Surgery length[a] Median [Interquartile range], minutes
Criteria A			
Total of participants	11 (25.6%) 2 (28.6%) 9 (25.7%)	0 [0-34] 0 [0-41] 0 [0-34]	356 [225-428] 547.5 [357-738] 350 [225-360]
Criteria B1			
Total of participants Frail participants Non-frail participants	31 (72.1%) 7 (100%) 23 (65.7%)	14 [0-46] 24 [14-68] 11 [0-46]	269 [199-360] 311 [139-542] 269 [208-360]
Criteria B2			
Total of participants Frail participants Non-frail participants	35 (81.4%) 6 (85.7%) 28 (80.0%)	18 [8-41] 28 [22-35] 14 [6-44]	259 [189-360] 334 [199-542] 258 [177-358]
Criteria A			

Legend:
[a] 10 missing values

All frail patients presented IOH when considering at least one of the criteria (Table 3).

Of non-frail patients, 82.9% (n=29) registered IOH. The difference between the two groups was not statistically significant (p=0.567).

It was verified that cumulative duration of IOH did not differ significantly between frail and non-fail groups, including after adjustment for age and sex, in generalized linear model. Frailty was not statistically significantly associated with the need of vasopressors in logistic regression analysis, even after adjusting for age and sex (Table 4).

POSTOPERATIVE DATA

At 30 days after surgery two frail patients had died (at 8 and 30 days postoperatively). All patients on the non-frail group were alive at the end of follow-up period. The overall survival rate was 96.2% and frailty had a significant influence on overall survival (p=<0.001) (Fig. 1).

Table 4. Association between frailty and vasopressors and cumulative duration of intraoperative hypotension

	Frailty state+			Frailty state*		
Outcome	**Non-Frail**	**Frail**	***p*-value**	**Non-frail**	**Frail**	***p*-value**
Vasopressors						
OR (CI 95%)	Reference	0.4 (0.1;2.2)	0.380	Reference	1.1 (0.1;8.4)	0.924
Cumulative duration						
B (CI 95%)	Reference	8.5 (-54.5;71.4)	0.688	Reference	-15.0 (-87.1;57.1)	0.675

Legend:
CI = confidence interval, OR = odds ratio, β= beta coefficcient
+raw data analysis
*adjusted for age, sex

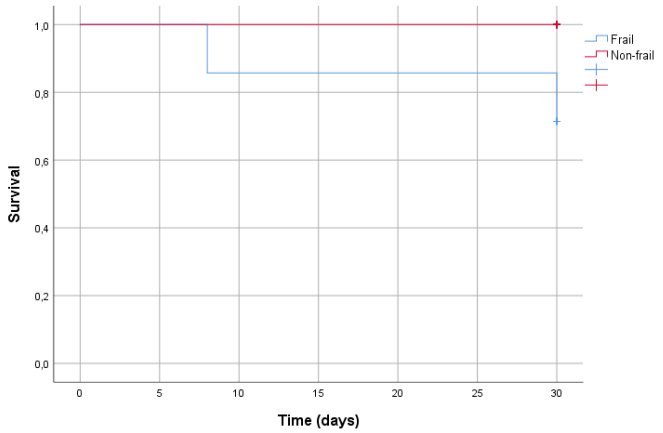

Figure 1. Kaplan-Meier survival analysis by frailty group; *p*=<0.001

DISCUSSION

It is recognized that frailty is associated with a progressive decline in different physiological systems, being viewed as a multidimensional condition because there is an interplay between physical and psychosocial factors in its development.[20]

Participants included in the study were mainly non-frail patients. In fact, only 13.7% of the 53 included patients were considered frail according to CFS ≥5, which is the cut-off most commonly used to describe frail people.[19] The use of a lower cut-off (≥4) to the screen of frailty prior to anesthesia, as advocated by some researchers, or the use of a more objective screening tool could lead to different results.[21]

However, CFS is an easy, quick and practical tool to screen frailty in every preoperative evaluation context that has demonstrated predictive value of poor clinical outcomes and mortality in older people, not requiring prolonged training for its consistent application.[19,22]

Previous reports indicate that frailty is more common in older people, with prevalence increasing with age, and in female gender, even though it can occur among non-elderly patients mainly if there are associated comorbidities.[1,23,24] In our study, median age was effectively higher in frail participants (p=0.022). Yet, despite the enrolled participants being mainly female (54.7%), frail patients were predominantly of male gender (85.7%, p=0.037), which is not in agreement with current literature.[24]

There are many recognized risk factors that can contribute to the development and progression of frailty. These comprise multiple domains, including socio-demographic, clinical, life-style-related and biological. In terms of clinical domain, two relevant risk factors include multimorbidity and polypharmacy, which were assessed in the present study.[20] Nonetheless, even though a greater prevalence of comorbidities as well as a higher number of patients with polypharmacy was verified in frail participants when compared with non-frail, there was not a significant association between these factors and presence of frailty.

In respect to the relationship between frailty and intraoperative complications, including IOH, there are not many studies published. Though, Leopold George NTN *et al* showed that frailty is associated with an increased risk of intraoperative complications such as hypotension, desaturation, need for vasopressors or blood transfusion.[25] In our study, there was not a statistically significant relationship between presence of frailty and the development as well as cumulative duration of IOH. The same was verified in relation to the use of vasopressors to treat hypotension even with adjustment for potential confounders. Still, all frail patients developed IOH when considering at least one of the criteria and criteria B1 was verified in 100% of frail patients in contrast with A and B2. The reduced sample of patients and the criteria used to define IOH may explain, in part, the lack of statistical evidence in the association of frailty and IOH. Actually, our results reinforce the need to establish a consensus definition of IOH once there is a wide range of criteria used in literature.[12,26]

Regarding the postoperative period, an association between frailty and postoperative mortality was described in previous reports in different timings and types of surgery.[27,28] In our study, frail patients presented a decreased survival at 30 days (96.2%) and frailty had a significant influence in overall survival in this period (p-value=<0.001). These findings support that association and endorse the increasing advocacy in literature to the routinely screening of frailty in the preoperative setting to identify frail patients, which have a decreased capacity to respond to the stress induced by the surgery. This early recognition of frailty can help to guide perioperative interventions directed at increasing the patient's physiological reserve and therefore improve their ability to cope with the stress of surgery and to minimize risks associated with these patients.[29,30]

One of the main limitations of this study was the small number of participants included. In fact, as mentioned above, this study was started shortly before COVID-19 was declared pandemic and subsequently conducted at a time when elective surgical activity was drastically reduced nationwide and selected patient' characteristics could be different from usual. A greater sample would improve our results and their external validity.

In conclusion, our study did not show an association between presence of frailty and an increased risk to the development of IOH, so this may constitute a topic of an extended investigation in time. However, it clearly demonstrates that frailty, evaluated by CFS, is associated with a decreased survival at 30 days postoperatively. In the author's view, it supports and outlights the routine use of CFS as a screening tool for frailty in perioperative care.

Ethical Disclosures
Conflicts of Interest: The authors have no conflicts of interest to declare.
Financing Support: This work has not received any contribution, grant or scholarship.
Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.
Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2013).
Provenance and Peer Review: Not commissioned; externally peer reviewed.

Responsabilidades Éticas
Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.
Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.
Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.
Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia revista em 2013 e da Associação Médica Mundial.
Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

Received: 4th of May, 2021 | Submissão: 04 de maio, 2021
Accepted: 24th of February, 2022 | Aceitação: 24 de fevereiro, 2022
Published: 24th of February, 2022 | Publicado: 24 de fevereiro, 2022

REFERENCES

1. Lin HS, McBride RL, Hubbard RE. Frailty and anesthesia - risks during and post-surgery. Local Reg Anesth. 2018;11:61-73. doi: 10.2147/LRA.S142996.
2. Shem Tov L, Matot I. Frailty and anesthesia. Curr Opin Anaesthesiol. 2017;30:409-17. doi: 10.1097/ACO.0000000000000456.
3. Bentov I, Kaplan SJ, Pham TN, Reed MJ. Frailty assessment: from clinical to radiological tools. Br J Anaesth. 2019;123:37-50. doi: 10.1016/j.bja.2019.03.034.
4. Ali TZ, Lehman EB, Aziz F. Modified Frailty Index can be used to predict adverse outcomes and mortality after lower extremity bypass surgery. Ann Vasc Surg. 2018;46:168-77. doi: 10.1016/j.avsg.2017.07.007.
5. Flexman AM, Charest-Morin R, Stobart L, Street J, Ryerson CJ. Frailty and postoperative outcomes in patients undergoing surgery for degenerative spine disease. Spine J. 2016;16:1315-23. doi: 10.1016/j.spinee.2016.06.017.
6. Panayi AC, Orkaby AR, Sakthivel D, Endo Y, Varon D, Roh D, et al. Impact of frailty on outcomes in surgical patients: A systematic review and meta-analysis. Am J Surg. 2019;218:393-400. doi: 10.1016/j.amjsurg.2018.11.020.
7. Shinall MC, Jr., Arya S, Youk A, Varley P, Shah R, Massarweh N, et al. Association of preoperative patient frailty and operative stress with postoperative mortality. JAMA Surg. 2019;155:e194620. doi: 10.1001/jamasurg.2019.4620.
8. Li JL, Henderson MA, Revenig LM, Sweeney JF, Kooby DA, Maithel SK, et al. Frailty and one-year mortality in major intra-abdominal operations. J Surg Res. 2016;203:507-12.e501.
9. George EL, Hall DE, Youk A, Chen R, Kashikar A, Trickey AW, et al. Association between patient frailty and postoperative mortality across multiple noncardiac surgical specialties. JAMA Surg. 2021;156:e205152. doi: 10.1001/jamasurg.2020.5152.
10. Parvaneh S, Howe CL, Toosizadeh N, Honarvar B, Slepian MJ, Fain M, et al. Regulation of Cardiac Autonomic Nervous System Control across Frailty Statuses: A Systematic Review. Gerontology. 2015;62:3-15.
11. Huang CJ, Kuok CH, Kuo TB, Hsu YW, Tsai PS. Pre-operative measurement of heart rate variability predicts hypotension during general anesthesia. Acta Anaesthesiol Scand. 2006;50:542-8.
12. Wesselink EM, Kappen TH, Torn HM, Slooter AC, van Klei WA. Intraoperative hypotension and the risk of postoperative adverse outcomes: a systematic review. Br J Anaesth. 2018;121:706-21. doi: 10.1016/j.bja.2018.04.036.
13. Sessler DI, Bloomstone JA, Aronson S, Berry C, Gan TJ, Kellum JA, et al. Perioperative Quality Initiative consensus statement on intraoperative blood pressure, risk and outcomes for elective surgery. Br J Anaesth. 2019;122:563-74. doi: 10.1016/j.bja.2019.01.019.
14. Walsh M, Devereaux PJ, Garg AX, Kurz A, Turan A, Rodseth RN, et al. Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery: toward an empirical definition of hypotension. Anesthesiology. 2013;119:507-15. doi: 10.1097/ALN.0b013e3182a10e26.
15. Mascha EJ, Yang D, Weiss S, Sessler DI. Intraoperative mean arterial pressure variability and 30-day mortality in patients having noncardiac surgery. Anesthesiology. 2015;123:79-91. doi: 10.1097/ALN.0000000000000686.
16. Kristensen SD, Knuuti J, Saraste A, Anker S, Botcker HE, De Hert S, et al. 2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). Eur Heart J. 2014;35:2383-431.
17. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373-83.
18. Lee TH, Marcantonio ER, Mangione CM, Thomas EJ, Polanczyk CA, Cook EF, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation. 1999;100:1043-9.
19. Church S, Rogers E, Rockwood K, Theou O. A scoping review of the Clinical Frailty Scale. BMC Geriatr. 2020;20:393. doi: 10.1186/s12877-020-01801-7.
20. Hoogendijk EO, Afilalo J, Ensrud KE, Kowal P, Onder G, Fried LP. Frailty: implications for clinical practice and public health. Lancet. 2019;394:1365-75. doi: 10.1016/S0140-6736(19)31786-6.
21. Darvall JN, Loth J, Bose T, Braat S, De Silva A, Story DA, et al. Accuracy of the Clinical Frailty Scale for perioperative frailty screening: a prospective observational study. Can J Anaesth. 2020;67:694-705. doi: 10.1007/s12630-020-01610-x.
22. Gregorevic KJ, Hubbard RE, Lim WK, Katz B. The clinical frailty scale predicts functional decline and mortality when used by junior medical staff: a prospective cohort study. BMC Geriatr. 2016;16:117. doi: 10.1186/s12877-016-0292-4.
23. Bottura C, Arcêncio L, Chagas HM, Evora PR, Rodrigues AJ. Frailty among non-elderly patients undergoing cardiac surgery. Arq Bras Cardiol. 2020;115:604-10. doi: 10.36660/abc.20190082.
24. Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community-dwelling older persons: a systematic review. J Am Geriatr Soc. 2012;60:1487-92.
25. Leopold-George NTN, Nethathe GD. Frailty in perioperative patients in three South African academic hospitals. S Afr Med J. 2019;109:535-40. doi: 10.7196/SAMJ.2019.v109i7.13439.
26. Bijker JB, van Klei WA, Kappen TH, van Wolfswinkel L, Moons KG, Kalkman CJ. Incidence of intraoperative hypotension as a function of the chosen definition: literature definitions applied to a retrospective cohort using automated data collection. Anesthesiology. 2007;107:213-20.
27. Sioutas G, Tsoulfas G. Frailty assessment and postoperative outcomes among patients undergoing general surgery. Surgeon. 2020;18:e55-e66. doi: 10.1016/j.surge.2020.04.004.
28. Tse W, Newton D, Amendola M, George M, Pfeifer J. Frailty index predicts long-term mortality and postoperative complications in patients undergoing endovascular aortic aneurysm repair. J Vasc Surg. 2020;72:1674-80. doi: 10.1016/j.jvs.2020.01.045.
29. Milder DA, Pillinger NL, Kam PCA. The role of prehabilitation in frail surgical patients: A systematic review. Acta Anaesthesiol Scand. 2018;62:1356-66.
30. Nidadavolu LS, Ehrlich AL, Sieber FE, Oh ES. Preoperative evaluation of the frail patient. Anesth Analg. 2020;130:1493-503. doi: 10.1213/ANE.0000000000004735.