Frailty and delirium in hospitalized older adults: A systematic review with meta-analysis

Highlights: (1) The prevalence of frailty in hospitalized older adults was 34% (from 23% to 46%). (2) The prevalence of delirium in hospitalized older adults was 21% (from 17% to 24%). (3) The relative risk of frailty and delirium was 1.66% (from 1.18% to 2.33%, \( p<0.001 \)). (4) Frailty is an independent risk factor for developing delirium. (5) Frailty can be a therapeutic target in the prevention of delirium.

Objective: to estimate the prevalence and synthesize diverse evidence about the relationship between frailty and delirium in hospitalized older adults. Method: a systematic review with meta-analysis in which observational studies conducted with older adults about frailty, delirium and hospitalization, were selected without time of language restrictions. The search was conducted in the MEDLINE, EMBASE, CINAHL, Scopus, Web of Science and CENTRAL databases during August 2021. The precepts set forth by the Joanna Briggs Institute (JBI) - Evidence Synthesis Groups were followed. The meta-analysis model estimated the relative risk corresponding to the prevalence of frailty and delirium. The inverse variance method for proportions was used to estimate the prevalence values and relative risks for binary outcomes. Results: initially, 1,244 articles were identified, of which 26 were included in the meta-analysis (\( n=13,502 \) participants), with 34% prevalence of frailty (95% CI:0.26-0.42; \( I^2=0.7618 \), \( p=0 \)) and 21% for delirium (95% CI:0.17-0.25; \( I^2=0.3454 \), \( p<0.01 \)). The risk for hospitalized older adults to develop delirium was 66% (RR: 1.66; 95% CI:1.23-2.22; \( I^2=0.4154 \), \( p<0.01 \)). Conclusion: 34% prevalence of frailty and 21% of delirium in hospitalized older adults, with frailty being an independent risk factor for developing delirium, with an increased chance of 66% when compared to non-frail individuals.

Descriptors: Systematic Review; Meta-Analysis; Hospitalization; Frail Elderly; Delirium; Prevalence.
Introduction

Older adults constitute a unique population segment in hospital care, and the assistance team must be aware of the particularities of this age group, especially the syndromes, in order to detect and treat them early in time\textsuperscript{(1)}\textsuperscript{,} Physical frailty deserves to be highlighted among such conditions due to its multicausal nature, being defined as follows: “a clinical condition characterized by increased vulnerability in the individual when exposed to internal and external stressors, and is a major contributor to functional decline and early mortality in older adults”\textsuperscript{(2)}\textsuperscript{.}

In the scoping review, 204 studies were evaluated on the theme of frail older adults hospitalized with acute diseases, 14\% from the geriatrics and emergency areas and 11\% from the general practice. Of the 204 studies, 67\% identified frail participants using the “Frailty Phenotype”, the “Clinical Frailty Scale” (CFS) and the “Frailty Index” (12\% each). In this review, 74\% of the studies showed a correlation between frailty and the “morality” and “hospitalization time” outcomes\textsuperscript{(3)}\textsuperscript{.}

Delirium is another condition that affects the hospitalized aged population. It is a form of acute brain dysfunction\textsuperscript{(4)} characterized by a sudden change in the level of attention and by an altered level of consciousness that fluctuates over time. The American Psychiatric Association’s definition, according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, is “a mental disorder of acute onset and fluctuating course characterized by disturbances of consciousness, orientation, memory, thinking, perception and behavior”\textsuperscript{(5)}\textsuperscript{.} It is associated with a decrease in functional status, to institutionalization, to premature mortality, and to an increase in health-related costs.

One-third of the clinical inpatients aged at least 70 years old have delirium; the condition is present in half of these patients on admission and develops during hospitalization in the other half\textsuperscript{(6)}\textsuperscript{.} Its etiology is multifactorial, with an incidence rate of 83\% in hospitalized older adults\textsuperscript{(7)}\textsuperscript{.}

Frailty and delirium share responsibility for the increase in morbidity and mortality\textsuperscript{(7)}\textsuperscript{,} in addition to prolonged hospitalization times and long-term functional and cognitive impairment\textsuperscript{(8)}\textsuperscript{.} In an emergency service, it was verified that delirium had 3 time more chances to occur in frail than in non-frail older adults after adjustments for age and gender\textsuperscript{(9)}\textsuperscript{.}

A prospective cohort study conducted in Italy with 89 hospitalized older adults evaluated delirium, attention performance and frailty status in a geriatric emergency department. To evaluate the patients’ attention, they were asked to list the months of the year backwards (MOTYB test), then list the days of the week backwards (DOWB) and count from 20 to 1 (BC). The mean age was 83.1 ± 6 years old and prevalence values of 47.19\% (n=42) and 41.70\% (n=37) were observed for frailty and delirium, respectively. There was an association between frailty and delirium (RR: 4.90; 95\% CI:2.01-11.94)\textsuperscript{(10)}\textsuperscript{.}

The association of the frailty level on admission to the emergency service with hospital complications, including delirium, was evaluated in the emergency room of two public general hospitals in Mexico City - Mexico. This secondary analysis of the cohort study conducted with 548 individuals presented a mean age of 76 ± 7.2 years old. The presence of delirium according to frailty stratification was 0\% (frailty index <0.2), 3.4\% (frailty index from 0.20 to 0.39), 6.2\% (frailty index from 0.40 to 0.59) and 23.2\% (frailty index >0.60); thus, frailty was positively associated with delirium (β = 3.68; 95\% CI: 1.53-5.83, p<0.01)\textsuperscript{(11)}\textsuperscript{.}

The literature regarding delirium and frailty in hospitalized older adults is scarce, being mainly limited to the mortality outcome or to specific subgroups such as hospital sectors or related to surgical procedures.

Relevance of the topic is noted due to the fact that physical frailty and delirium proved to be two of the most complex management problems among hospitalized older adults. In the clinical practice, occurrence of these conditions is constantly observed among hospitalized older adults, and they are related to negative outcomes such as delayed functional recovery, disability\textsuperscript{(12)}\textsuperscript{and death\textsuperscript{(13)}\textsuperscript{.}}

Given the above, the objective of the current study was to estimate the prevalence and synthesize diverse evidence about the relationship between frailty and delirium in hospitalized older adults.

Method

This is a systematic review with meta-analysis, based on the precepts set forth by the Joanna Briggs Institute (JBI) – Evidence Synthesis Groups\textsuperscript{(14)}\textsuperscript{.} The “Association of delirium and fragility in hospitalized elderly: systematic review” protocol is published on the International Platform of Registered Systematic Review and Meta-analysis Protocols (INPLASY), DOI: 10.37766/inplasy2021.9.0022.

Research strategy

In order to formulate the guiding question and design the search for studies, the PEO (P – Population or Patients; E – Exposure; O – Outcomes)\textsuperscript{(15)}\textsuperscript{ was used, where P (Frail older adults), E (Hospitalization) and O (Delirium). After applying the PEO strategy, and to guide the search strategy terms, the following question was formulated: Which is the relationship between frailty and delirium in hospitalized older adults?
The inclusion criteria to select the study were as follows: observational studies, including prospective and retrospective cohort, case-control and cross-sectional studies; presence of the variables of interest: “frailty” and “delirium”; developed in a hospital setting; involving older adults aged ≥ 60 years old; and published in any language with no limitation regarding publication date. The exclusion criteria for the studies were as follows: not categorizing patients as frail and non-frail, case reports, letters to the editor, abstracts in conference proceedings, dissertations, theses and monographs.

Search and selection of the studies

The search strategy was specific to each database and initially used the Medical Subject Headings (MeSH) descriptors, later translated into specific descriptors (Descritores em Ciências da Saúde, DeCS) and Embase Subject Headings (Emtree). The search strategy was applied by the main researcher in the MEDLINE (PubMed Portal); SciELO; BVJ; EMBASE; CINAHL; Scopus; Web of Science (CAPES Journals Portal) and CENTRAL (Cochrane) databases in August 2021; the following search terms (MeSH): Aged, Frailty, Frail Elderly, Inpatients, Delirium, Hospitalization and the free terms: Elderly, Frailties, Frailness, Frailty Syndrome, Debilities, Functionally Impaired Elderly, Frail Older Adults, Subacute Delirium, Mixed Origin Delirium were associated by means of the Boolean operators (OR and AND) and structured the specific search strategy for each database, as described in the systematic review protocol registration.

Data extraction and synthesis

The total number of articles found in each database and the sum of all databases were recorded in the PRISMA flowchart,(16) as well as the entire selection process and reasons for exclusion. The results of the searches were imported into the Mendeley® software to store, organize and classify the references. In addition to that, it was possible to remove the duplicates in the reference manager.

The database search was performed by the main researcher, who then divided the titles of the articles between two reviewers who performed the evaluation independently.

The titles of the articles were analyzed and the ineligible studies were excluded. In the subsequent stage, the abstracts were read and the ineligible articles were removed after applying the eligibility criteria.

The abstracts evaluated were returned to the main researcher, who made all articles available in full-text format to the reviewers for evaluation of the eligibility criteria. To minimize a possible bias in selection of the studies, a refinement procedure was performed by two independent reviewers seeking 100% agreement, and a third reviewer evaluated the possible divergences that occurred in the selection of abstracts to make a final decision on their inclusion or exclusion.

Data extraction was performed in a Microsoft Excel® table to compile the data from the studies included. It was constructed to cover the previously defined eligibility criteria using the Joanna Briggs Institute(14) instruments, which included the following: author’s name, year, country, patient’s profile, purpose of the paper, sample size, study design, frailty evaluation instrument, delirium evaluation instrument and outcomes. The final references of the primary studies included were also evaluated manually, in an attempt to find relevant articles that might be added to the review.

To describe the intensity of agreement between the reviewers, the Kappa measure was used, which is based on the number of concordant answers, i.e., the frequency at which the result is the same between the reviewers(17). For this study, the Kappa agreement index was 0.892, which shows strong/ almost perfect agreement between the reviewers.

The data analyzed for the meta-analysis were the following: total number of patients, number of frail and non-frail patients, number of patients with delirium and their combined effects. The meta-analysis model estimated the relative risk corresponding to the prevalence of frailty and delirium. The “pooled effects” were estimated using the inverse variance method of proportions to estimate prevalence values and relative risk for the binary outcomes, with 95% confidence interval, and represented in Forest plots.

Heterogeneity across the studies was tested by means of the I² test, considering it significant when $p<0.05$. The alternative hypothesis of the heterogeneity test is that variability/heterogeneity is significant; therefore, fixed or random effects models were chosen based on acceptance or rejection of the null hypothesis. All the analyses were performed in the R 4.1.1 environment(18).

Evaluation of the methodological quality

The eligible studies were critically evaluated by two independent reviewers regarding their methodological quality by resorting to the Joanna Briggs Institute (JBI) scale. Any and all disagreements were solved by means of a discussion with a third reviewer. On a scale consisting of nine criteria, studies that met from zero to three criteria were considered to be of low quality, those that met from four to six criteria were considered to be of medium quality, and from seven or more were considered to be of high methodological quality. The evaluation scores in relation to the methodological quality showed that most
of the articles are of average to high quality. Regardless of the results referring to their methodological quality, all the articles were submitted to data extraction and synthesis, as can be seen in Figure 1.

| AUTHOR (DATE)             | 1. Is the sample clipping appropriate to address the target population? | 2. Were the study participants properly sampled? | 3. Was the sample size adequate? | 4. Were the study participants and design described in detail? | 5. Was data analysis performed with sufficient sample coverage? | 6. Were valid methods used to identify the condition? | 7. Was the condition assessed in a standardized and reliable way? | 8. Was an appropriate statistical analysis performed? | 9. Was the response rate adequate and, if not, was the low response rate properly managed? | Total |
|--------------------------|-------------------------------------------------|-------------------------------------------------|---------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|------|
| Leung; Tsai; Sands, 2011 | (-)                                             | (+)                                             | (-)                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+) | 7 |
| Eeles et al., 2012       | (+)                                             | (+)                                             | (-)                             | (-)                                             | (+)                                             | (+)                                             | (+)                                             | (-)                                             | (+)                                             | (+) | 6 |
| Joosten et al., 2014     | (+)                                             | (U)                                             | (+)                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (U)                                             | (+) | 8 |
| Hempenius et al., 2014   | (-)                                             | (+)                                             | (+)                             | (+)                                             | (+)                                             | (U)                                             | (+)                                             | (+)                                             | (+)                                             | (+) | 7 |
| Eide et al., 2015        | (+)                                             | (+)                                             | (-)                             | (+)                                             | (+)                                             | (U)                                             | (+)                                             | (+)                                             | (+)                                             | (+) | 7 |
| Partridge et al., 2015   | (+)                                             | (+)                                             | (+)                             | (+)                                             | (U)                                             | (+)                                             | (U)                                             | (+)                                             | (+)                                             | (+) | 8 |
| Nguyen; Cumming; Hilmer, 2016 | (-)                                             | (+)                                             | (+)                             | (+)                                             | (+)                                             | (+)                                             | (U)                                             | (+)                                             | (+)                                             | (+) | 7 |
| Assmann et al., 2016     | (-)                                             | (+)                                             | (-)                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+) | 7 |
| Chew et al., 2017        | (+)                                             | (+)                                             | (+)                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+) | 9 |
| Ogawa et al., 2017       | (+)                                             | (+)                                             | (+)                             | (+)                                             | (+)                                             | (+)                                             | (-)                                             | (+)                                             | (+)                                             | (+) | 7 |
| Gleason et al., 2017     | (-)                                             | (+)                                             | (+)                             | (+)                                             | (U)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+) | 7 |
| Dani et al., 2018        | (+)                                             | (+)                                             | (+)                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+) | 9 |
| Tanaka et al., 2018      | (+)                                             | (+)                                             | (+)                             | (+)                                             | (+)                                             | (+)                                             | (U)                                             | (+)                                             | (+)                                             | (+) | 8 |
| Giroux et al., 2018      | (+)                                             | (+)                                             | (-)                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+) | 7 |
| Alabaf Sabbagh i et al., 2018 | (+)                                             | (+)                                             | (+)                             | (+)                                             | (+)                                             | (+)                                             | (-)                                             | (U)                                             | (+)                                             | (-) | 6 |
| Nomura et al., 2018      | (-)                                             | (+)                                             | (-)                             | (+)                                             | (+)                                             | (+)                                             | (U)                                             | (+)                                             | (+)                                             | (+) | 6 |
| Goudzwaard et al., 2018  | (-)                                             | (+)                                             | (-)                             | (+)                                             | (+)                                             | (U)                                             | (+)                                             | (+)                                             | (+)                                             | (+) | 6 |
| Geriatric Medicine Research Collaborative, 2019 | (+)                                             | (+)                                             | (+)                             | (-)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+) | 8 |
| Saravana-Bawan et al., 2019 | (+)                                             | (+)                                             | (+)                             | (+)                                             | (+)                                             | (+)                                             | (U)                                             | (+)                                             | (+)                                             | (+) | 8 |
| Bello et al., 2019       | (-)                                             | (+)                                             | (-)                             | (+)                                             | (+)                                             | (+)                                             | (U)                                             | (+)                                             | (+)                                             | (+) | 6 |
| Goudzwaard et al., 2020  | (+)                                             | (+)                                             | (+)                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+) | 9 |
| Itagaki et al., 2020     | (+)                                             | (+)                                             | (-)                             | (+)                                             | (+)                                             | (U)                                             | (+)                                             | (-)                                             | (+)                                             | (+) | 6 |
| Salju et al., 2020       | (+)                                             | (+)                                             | (+)                             | (-)                                             | (+)                                             | (U)                                             | (+)                                             | (+)                                             | (+)                                             | (+) | 7 |
| Susho et al., 2020       | (+)                                             | (+)                                             | (+)                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+) | 8 |
| Mahanna-Gabrielli et al., 2020 | (+)                                             | (+)                                             | (+)                             | (+)                                             | (U)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+) | 8 |
| Chen; Qin, 2020         | (+)                                             | (+)                                             | (+)                             | (-)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+)                                             | (+) | 7 |

Note: (-) Did not meet this criterion; (+) Met this criterion; (U) Uncertain/Not clear. The score varies between 0 and 9 and, the higher it is, the better the quality of the study.

Figure 1 - Result of the methodological evaluations of the articles included in the study. Curitiba, PR, Brazil, 2021
Ethical aspects

As this study resorted to articles from databases and did not involve human beings, it waived approval by the Research Ethics Committee, according to National Health Council Resolution No. 510/2016 and the ethical regulations in force\(^{42}\).

Results

The database search resulted in 1,244 studies in all eight databases; 748 were excluded for being duplicates and 496 were selected for reading their titles and abstracts. Of these, 398 articles were excluded after reading their titles and 21 after reading the abstracts, resulting in the selection of 77 for full-reading. A total of 51 were excluded after this stage, resulting in the inclusion of 26 articles. No new eligible studies for the review were found after consulting the references of the primary studies. Figure 2 shows the flowchart of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) method used to illustrate selection of the articles for this systematic review\(^{16}\).

![PRISMA flowchart](image)

Figure 2 – PRISMA flowchart corresponding to selection of the studies. Curitiba, PR, Brazil, 2021

The reviewers included all the studies that met the inclusion and exclusion criteria, with discussion of the methodological weaknesses. A total of 13,502 participants (minimum of 63, maximum of 6,191) were included in the meta-analysis, with predominance of publications in 2019 and 2020 (n=5; 19.25%); 2018 (n=4; 15.38%); 2015 and 2017 (n=3; 11.55%); 2016 (n=2; 7.70%); and in 2011, 2012, 2014 and 2021 (n=1; 3.85%).

The following stand out among the countries where the studies were conducted: United States of America (n=5; 19.23%), followed by Japan (n=4; 15.38%), the Netherlands (n=4; 15.38%), United Kingdom
(n=4; 15.38%), Canada (n=2; 7.69%), Australia (n=2; 7.69%), Singapore (n=1; 3.84%), Norway (n=1; 3.84%), Italy (n=1; 3.84%), China (n=1; 3.84%) and Belgium (n=1; 3.84%).

The most commonly employed frailty evaluation instrument was the Frailty Index (n=5; 19.23%); followed by the Clinical Frailty Scale (CFS) (n=4; 15.38%); the Frail Scale (n=3; 11.53%), the Erasmus Frailty Score (EFS), the Edmonton Frail Scale (n=2; 7.69%), the Japanese CHS version (j-CHS), the Kihon Checklist, the Frailty Index associated with clinical judgment; Groningen Frailty Indicator; Handgrip strength and gait speed; Erasmus Frailty Score, the Cardiovascular Health Study (CHS), Fried's phenotype and modified Fried's criteria (n=1; 3.84%).

The most commonly used instrument for evaluation of delirium was the Confusion Assessment Method (CAM) (n=8; 30.75%); followed by the Intensive Care Delirium Screening Checklist (ICDSC) (n=3; 11.54%); uninform ed (n=3; 11.54%); geriatric clinical evaluation (n=2; 7.70%); Diagnostic and Statistical Manual of Mental Disorders fifth edition (DSM-5) (n=2; 7.70%); Abbreviated Mental Test - 4 (4-ATM)/DSM-5 (n=2; 7.70%) and severity evaluation of the Delirium Rating Scale-Revised-98 (DRS-R-98), 4-ATM score, Confusion Assessment Method for the Intensive Care Unit (CAM-ICU), CAM/CAM-ICU, CAM/DSM-5, DSM-4 and (n=1; 3.35%).

Figure 3 shows the distribution of the characteristics of the studies that comprised the corpus of the systematic review, with the following variables: author's name, year, country, patient's profile, objective of the paper, sample size, study design, frailty evaluation instrument, delirium evaluation instrument and outcomes.

| Authors | Origin | Type of patients | Objective | Sample size | Type of study | Age | Instrument for frailty | Instrument for delirium | Results (95% CI) |
|---------|--------|-----------------|-----------|-------------|---------------|-----|----------------------|----------------------|-----------------|
| Leung; Tsai; Sands, 2011†† | USA | Surgical, non-cardiac | To investigate if preoperative frailty in surgical non-cardiac patients favors onset of postoperative delirium. | 63 | Prospective cohort study | >65 years old | Modified Fried Criteria | CAM | Prevalence of frailty HR: 0.33 (0.23 – 0.45) Prevalence of delirium HR: 0.25 (0.16 – 0.37) Risk of delirium in frail patients RR: 2.57 (1.11 – 5.94) |
| Eeles, et al., 2012‡‡ | Australia | Acute care, general hospital | To explore the relationship between delirium and frailty in aged patients and to determine their impact on survival. | 273 | Prospective cohort study | 82.3±7.5 | FFI (33 items) (Frail=0.25) | DSM-5 § | Prevalence of frailty HR: 0.41 (0.35 – 0.47) Prevalence of delirium HR: 0.37 (0.31 – 0.43) Risk of delirium in frail patients RR: 3.62 (2.54 – 5.18) |
| Joosten, et al., 2014‡‡ | Belgium | Geriatric ward | To evaluate the prevalence of frailty and to determine to which extent it predicts delirium, falls and mortality in hospitalized aged patients. | 220 | Prospective cohort study | CHS*: Frail 83.3±5.4 SOFI††: 83.1±5.2 | CHS* and SOFI†† | CAM | Prevalence of frailty HR: 0.40 (0.34 – 0.47) Prevalence of delirium HR: 0.11 (0.08 – 0.16) Risk of delirium in frail patients RR: 1.07 (0.50 – 2.30) |
| Hempenius, et al., 2014‡‡ | Netherlands | Surgery, solid tumors | To determine the risk factors for postoperative delirium (POD) in aged patients with cancer. | 251 | Multicenter and retrospective cohort study | 74.2±6.4 (65 – 92) | Groningen Frailty Indicator | CAM | Prevalence of frailty HR: 0.34 (0.23 – 0.34) Prevalence of delirium HR: 0.18 (0.14 – 0.24) Risk of delirium in frail patients RR: 2.01 (1.20 – 3.37) |

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| Authors                  | Origin                  | Type of patients                                      | Objective                                                                 | Sample size | Type of study | Age            | Instrument for frailty | Instrument for delirium | Results (95% CI)          |
|-------------------------|-------------------------|-------------------------------------------------------|--------------------------------------------------------------------------|-------------|---------------|-----------------|------------------------|--------------------------|---------------------------|
| Partridge, et al., 2015 | United Kingdom          | Elective and emergency arterial-vascular surgeries   | To evaluate the prevalence of frailty, clinical conditions and functional status in preoperative among older adults undergoing arterial vascular surgery and to evaluate postoperative outcomes. | 125         | Prospective cohort study | 76.3 ± 7.27 | EFS* (Frail≤6.5) | Not reported           | Prevalence of frailty HR: 0.52 (0.43 – 0.61) Prevalence of delirium HR: 0.15 (0.10 – 0.22) Risk of delirium in frail patients RR: 0.27 (0.17 – 0.43) |
| Nguyen; Cumming; Hilmer, 2016 | Australia              | Clinical                                              | To investigate the impact of frailty on mortality, hospitalization time and readmission in hospitalized aged patients with arterial fibrillation. | 302         | Prospective cohort study | 84.7 ± 7.1   | EFS†††            | Not reported            | Prevalence of frailty HR: 0.53 (0.48 – 0.59) Prevalence of delirium HR: 0.10 (0.07 – 0.14) Risk of delirium in frail patients RR: 1.00 (0.51 – 1.98) |
| Assmann, et al., 2016   | Netherlands             | Cardiac surgery (TAV†††)                              | To evaluate frailty as an indicator to predict delirium and mortality after TAV††. | 89          | Prospective cohort study | 80.4           | FI and Clinical judgment | DSM-4‡‡‡                  | Prevalence of frailty HR: 0.53 (0.43 – 0.63) Prevalence of delirium HR: 0.28 (0.20 – 0.38) |
| Chew, et al., 2017      | Singapore               | Surgical                                              | To investigate the association between frailty and incomplete recovery from delirium at discharge and to examine the mediating role of incomplete recovery in the relationship between frailty and functional recovery 12 months after delirium. | 234         | Prospective cohort study | 84.1 ± 7.1   | FI (20 items) (Frail=0.25) | DRS-R-98§§              | Prevalence of frailty HR: 0.68 (0.62 – 0.74) Prevalence of delirium HR: 0.23 (0.18 – 0.28) Risk of delirium in frail patients RR: 0.90 (0.84 – 0.98) |
| Ogawa, et al., 2017     | Japan                   | Cardiac surgery                                       | To examine the associations between delirium and postoperative frailty and major cardiac adverse events. | 326         | Prospective cohort study | 68.6 ± 14.8  | Handgrip strength and gait speed | ICDSC‡              | Prevalence of frailty HR: 0.07 (0.04 – 0.10) Prevalence of delirium HR: 0.13 (0.10 – 0.17) Risk of delirium in frail patients RR: 3.16 (1.67 – 5.96) |
| Gleason, et al., 2017   | USA                     | Orthopedic surgery and Geriatrics service             | To stratify frailty in older adults admitted with fractures to determine its association with the postoperative results. | 175         | Retrospective cohort study | 82.3 ± 7.4   | FRAIL                | Not performed            | Prevalence of frailty HR: 0.42 (0.35 – 0.49) Prevalence of delirium HR: 0.20 (0.15 – 0.27) Risk of delirium in frail patients RR: 0.48 (0.26 – 0.87) |
| Dani, et al., 2018      | United Kingdom          | Emergency Sector                                      | To evaluate the impact of delirium on mortality in a cohort evaluated for frailty. | 710         | Prospective cohort study | 83.1 ± 7.4   | FI (31 items) | CAM†                   | Prevalence of delirium HR: 0.10 (0.08 – 0.13) |
| Tanaka, et al., 2018    | Japan                   | Liver resection surgery                               | To apply the Kihon Checklist to evaluate preoperative frailty in older adults to predict outcomes after liver resection. | 217         | Multicenter and prospective cohort study | 75 frail and age 72 non-frail people | KC*** (Frail=8) | ICDSC‡‡‡                 | Prevalence of frailty HR: 0.29 (0.23 – 0.35) Prevalence of delirium HR: 0.12 (0.09 – 0.17) Risk of delirium in frail patients RR: 6.52 (1.79 – 23.78) |

Authors                  | Origin                  | Type of patients                                      | Objective                                                                 | Sample size | Type of study | Age            | Instrument for frailty | Instrument for delirium | Results (95% CI)          |
|-------------------------|-------------------------|-------------------------------------------------------|--------------------------------------------------------------------------|-------------|---------------|-----------------|------------------------|--------------------------|---------------------------|
| Giroux, et al., 2018    | Canada                  | Emergency Sector                                      | To evaluate frailty screening in older adults in the Emergency Department can help identify the risk of delirium. | 335         | Prospective cohort study | 76.8 ± 8.1 | CFS§§ (Frail=5%) | CAM††                  | Prevalence of frailty HR: 0.21 (0.17 – 0.26) Prevalence of delirium HR: 0.12 (0.09 – 0.16) Risk of delirium in frail patients RR: 3.79 (2.16 – 6.63) |

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| Authors                              | Origin            | Type of patients               | Objective                                                                 | Sample size | Type of study          | Age        | Instrument for frailty | Instrument for delirium | Results (95% CI)                      |
|--------------------------------------|-------------------|-------------------------------|---------------------------------------------------------------------------|-------------|-------------------------|------------|------------------------|--------------------------|--------------------------------------|
| Alabaf Sabbaghi, et al., 2018         | United Kingdom    | Emergency Sector              | To compare the clinical characteristics, frailty, dementia and delirium in a specialized counseling team for frail older adults versus usual treatment. | 6,191       | Retrospective and documentary | 84.6±6.3  | CFS ¹², ⁴-ATM¹³        | CAM         | Prevalence of frailty HR 0.05 (0.04 – 0.06) Prevalence of delirium HR 0.12 (0.11 – 0.13) |
| Nomura, et al., 2018                  | Japan             | Cardiac surgery               | To examine the hypothesis that baseline frailty would be associated with postoperative delirium and to cognitive changes from 1 to 12 months after a cardiac surgery. | 133         | Prospective cohort study | Robust 69.3±7.9 Fried's Phenotype CAM¹⁴ and CAM-ICU¹⁵ | 73.4±8.09 |                        |                                         | Prevalence of frailty HR 0.34 (0.26 – 0.42) Prevalence of delirium HR 0.48 (0.40 – 0.58) Risk of delirium in frail patients RR 1.04 (0.68 – 1.58) |
| Goudzwaard, et al., 2018              | Netherlands       | Cardiac surgery (TAVI)        | To investigate the association between a new Erasmus Frailty Score and short- and long-term results after TAVI. | 213         | Prospective cohort study | 82.0 (IGR: 78.2 – 85.6) Erasmus Frailty Score (>3/5 of the domains) Geriatric clinical evaluation | ⁴-ATM¹³ and DSM-5⁵ |                        |                                         | Prevalence of frailty HR 0.66 (0.64 – 0.68) Prevalence of delirium HR 0.15 (0.13 – 0.17) Risk of delirium in frail patients RR 2.83 (2.21 – 3.62) |
| Geriatric Medicine Research Collaborative, 2019 | United Kingdom    | Emergency Sector              | To evaluate frailty and the patient’s/hospital’s risk factors for delirium. | 150⁷        | ⁴-ATM¹³ and DSM-5⁵       | 80.0±8.3  | CFS¹¹                  | CAM⁴                    | Prevalence of frailty HR 0.24 (0.20 – 0.29) Prevalence of delirium HR 0.23 (0.19 – 0.28) Risk of delirium in frail patients RR 2.68 (1.76 – 3.79) |
| Saravana-Bawan, et al., 2019          | Canada            | Emergency general surgery     | To evaluate the incidence and risk factors of delirium in older adults subjected to emergency surgeries. | 332         | Prospective cohort study | 76.1±7.66 | CFS¹¹                  | CAM⁴                    | Prevalence of frailty HR 0.24 (0.20 – 0.29) Prevalence of delirium HR 0.23 (0.19 – 0.28) Risk of delirium in frail patients RR 2.68 (1.76 – 3.79) |
| Bellegli, et al., 2019                | Italy             | Acute care (Geriatric emergency) | To evaluate if frailty is associated with delirium and if it affects performance in three attention tests. | 89          | Prospective cohort study | 83.1±6.05 | CAM⁴                  | CAM⁴                    | Prevalence of frailty HR 0.28 (0.25 – 0.32) Prevalence of delirium HR 0.14 (0.11 – 0.17) Risk of delirium in frail patients RR 2.22 (1.44 – 3.42) |
| Goudzwaard, et al., 2020              | Netherlands       | Cardiac surgery (TAVI)        | To investigate the incidence, the determinants and the consequences of postoperative delirium in aged patients subjected to TAVI. | 543         | Prospective cohort study | 79.1±8.0  | Erasmus Frailty Score (<3/5 of the domains) Geriatric clinical evaluation |CAM⁴| Prevalence of frailty HR 0.28 (0.25 – 0.32) Prevalence of delirium HR 0.14 (0.11 – 0.17) Risk of delirium in frail patients RR 2.22 (1.44 – 3.42) |
| Itagaki, et al., 2020                 | Japan             | Cardiac surgery               | To examine how physical frailty and cognitive impairment affect the incidence of delirium after cardiac surgeries in older patients. | 89          | Retrospective study     | 74.9±5.5  | j-CHS¹⁰          | ICDSC¹¹       | Prevalence of frailty HR 0.27 (0.19 – 0.37) Prevalence of delirium HR 0.35 (0.26 – 0.45) Risk of delirium in frail patients RR 2.51 (1.24 – 5.08) |
| Saljuqi, et al., 2020                 | USA               | Emergency general surgery     | To evaluate the impact of frailty on delirium and on other outcomes in geriatric patients subjected to emergency general surgeries. | 163         | Prospective cohort study | 7±7       | EGSSFI¹⁷        | CAM⁴                    | Prevalence of delirium HR 0.26 (0.20 – 0.33) Risk of delirium in frail patients RR 2.50 (1.50 – 4.17) |

(continues on the next page...)
In Figure 4, it can be seen that the prevalence of frailty in the combined effect of all studies was 34% (from 26% to 42%) $I^2=99%$; $t^2=0.7618$, $p=0$, and that the value for delirium was 21% (from 17% to 25%), with $I^2=95%$; $t^2=0.3454$, $p<0.01$. 

Figure 3 - Distribution of the characteristics of the studies that comprised the corpus of the systematic review. Curitiba, PR, Brazil, 2021
In Figure 5, the relative risk of frailty and delirium was 1.66 (from 1.18 to 2.22; $I^2=92\%$; $t^2=0.4154$, $p<0.01$). Each line represents a study, and the last one represents the combination of the results (meta-analysis), which is symbolized by a “diamond”.

Note: Heterogeneity was tested by means of the $I^2$ test, considering it significant when $p<0.05$. *CI = Confidence Interval

Figure 4 - Estimated prevalence of physical frailty and delirium in the meta-analysis model. Curitiba, PR, Brazil, 2021
Discussion

In this systematic review with meta-analysis, it was identified that frailty was independently associated with an increased risk of delirium in hospitalized older adults: 1.66 (95% CI: 1.23-2.22; I²=95%; t²=0.4154, p<0.01). The prevalence of frailty in hospitalized older adults was 34% (from 26% to 42%) and that of delirium across the studies was 21% (from 17% to 25%).

The scarcity of studies evaluating frailty as a predisposing factor to delirium[10,21,37-38,41] was an unexpected finding of this paper, as the association between these conditions is accepted in the clinical practice. No relationship was observed between frailty and development of delirium in seven of the 26 studies analyzed, (RR: 1; 95% CI: 0.51-1.98)[29], (RR: 0.90; 95% CI: 0.36-2.23)[21], (RR: 0.48; 95% CI: 0.26-0.87)[29], (RR: 1.04; 95% CI: 0.68-1.54)[32], (RR: 1.14; 95% CI: 0.85-1.53)[23], (RR: 0.90; 95% CI: 0.84-0.98)[27], (RR: 0.27; 95% CI: 0.17-0.43)[24].

The instruments used to evaluate frailty showed great heterogeneity, with preference given to the use of multidimensional instruments. Evaluation by Fried’s frailty phenotype[32] was used in only one study; however, its markers were used in other studies, which worked with Fried’s modified phenotype[19], or some of its components (gait speed and handgrip strength)[28]. Only one of the studies used a frailty index associated with clinical judgment[26].

Delirium was evaluated using validated diagnostic instruments and screening tools, with significant heterogeneity across the studies. The screening instrument most frequently used was the Confusion Assessment Method (CAM)[9,13,15,21-23,35,38]. Other studies have used the association of CAM with other instruments, such as CAM-ICU[32] and/or DSM diagnostic criteria[38]. Used in critically-ill patients, CAM-ICU was also used separately[39].

4-AT, a faster evaluation instrument, was used separately[31] or associated with the DMS-V criteria[10,34]. The diagnostic criteria were used alone, DMS-IV[25], and/or associated with other POD/DMS-V criteria[41]. Other ways of detecting delirium were employed, such as geriatric evaluation[33,36] and ICDSC[28,30,37]. Some studies did not specify the detection method[24,29].

The prevalence of frailty in hospitalized older adults was 34% (from 23% to 46%). The highest prevalence values of frailty were observed in a study conducted in Singapore with 234 older adults with surgical indication in which the association between frailty and residual subsyndromic delirium was investigated: 68% (from 62% to 74%)[27]. The prospective multicenter study conducted in 45 hospitals from the United Kingdom with a sample of 1,507 patients also reached high percentages of frailty and values close to the study developed in Singapore: 66% (from 64% to 68%)[34].

A number of studies developed in China and Australia have found slightly lower percentages of frailty when compared to the aforementioned studies. In China, with a sample consisting of 383 older adults, the study aimed...
at examining the MFI discriminatory value to predict delirium and cognitive dysfunction after hip arthroplasty, and 54% (from 62% to 74%) prevalence was observed\(^\text{40}\). In Australia, the study developed with 302 aged patients hospitalized with atrial fibrillation showed 53% (from 48% to 59%) prevalence\(^\text{25}\).

The prevalence of delirium among the studies was 21% (from 17% to 24%). The highest prevalence observed was found in the study conducted in Japan, 48% (95% CI: 40%-56%), with 133 patients that evaluated the association of baseline frailty with postoperative delirium and cognitive change 1 and 12 months after cardiac surgeries\(^\text{22}\). In the prospective cohort study conducted in Italy with 89 older adults, evaluating frailty and delirium in patients admitted to a geriatric emergency service, the prevalence of delirium was 42% (from 32% to 52%)\(^\text{10}\).

The mechanisms surrounding development of delirium in frail patients are complex: these patients experience decreased functional capacity and increased vulnerability when subjected to a stressor, such as major surgery or an acute critical medical situation, making it more likely that they will experience delirium. Frail older adults also have cognitive impairment, which intensifies the risk of delirium\(^\text{12}\).

From a clinical point of view, frailty can be considered a risk factor for development of delirium, although there is still not sufficient evidence that delirium can be a trigger for frailty. When persistent, delirium can be a precipitating factor for deterioration in terms of frailty. In the evaluation of the hospitalized older adults, frailty should be screened for, as it allows anticipating occurrence of delirium. Likewise, systematic screening for delirium should be performed to identify individuals at risk for subsequent deterioration in terms of frailty\(^\text{43}\).

Active search for the frailty condition in the acute care setting (hospitalized patients) is mandatory, and an individualized approach is required in the management of frail older adults\(^\text{44}\), due to the higher association with hospital complications\(^\text{43}\).

A cohort study conducted with 710 older adults in a hospital with patients over 70 years old evidenced that both delirium and frailty independently increase the risk of death, delirium (HR: 2.4; 95% CI: 1.8-3.3, \(p<0.01\)) and frailty (HR 3.5, 95% CI: 1.2-9.9, \(p=0.02\)). The risk of death is higher in patients with delirium at all frailty levels, which highlights the importance of preventing, detecting and treating delirium in any patient and recognizing it as a serious condition that interferes with prognosis\(^\text{15}\).

Frailty is a dynamic entity, and older adults can transition from being robust to being frail\(^\text{46}\). Little is said about the specific approach to physical frailty in the hospitalized patient, with its relationship to morbidities, mortality, and/or delirium being more evaluated. A comprehensive care plan for frailty should systematically address the following: polypharmacy, management of sarcopenia, treatable causes of weight loss and causes of exhaustion (depression, anemia, hypotension, hypothyroidism, and vitamin B12 deficiency), with strong recommendation, although with too low certainty of evidence\(^\text{47}\).

Although more studies are needed to better clarify the cause/effect relationship between these two conditions, this association has important clinical implications. The presence of frailty should be investigated in hospitalized aged patients, as this condition predicts negative adverse outcomes and requires individualized care. When present, frailty should lead to a search for the presence of concomitant delirium, given the high probability of its simultaneous incidence. In the absence of delirium, evidence-based non-pharmacological measures should be intensively implemented to prevent it\(^\text{48}\), given the high risk for its development.

Programs involving multiple components conducted by different professionals in the prevention of delirium have the potential to reduce complications in high-risk aged patients, thereby improving treatment and long-term quality of life. The implementation of additional interprofessional teams acting to prevent delirium and providing regular training on the optimal management of delirium is an intervention option. Demonstrating the effectiveness of these programs requires large multicenter studies\(^\text{49}\).

The methodological quality of the studies was evaluated as reasonable to good (not excellent) and they were heterogeneous with regard to study populations and definitions of the variables of interest (frailty and delirium). The quality levels of the studies evaluated did not influence the association between frailty and subsequent delirium, but the risk of bias was relevant because many studies did not adjust for confounding factors. Most of the studies included in the current systematic review evidenced the association between the frailty and delirium variables, and it is up to health professionals to evaluate older adults with adequate instruments to detect the frailty syndrome associated with development of delirium.

The strengths of this study include the comprehensive search strategy, the methodological evaluation, and the standardized data extraction process. The limitations of this systematic review are the heterogeneous and specific populations of the studies included, the sample sizes (not always representative of the population), and the different methods to evaluate frailty and delirium.

The dichotomous evaluation of frailty and delirium may be another bias, as these conditions can be classifiable in terms of severity. Another possible limitation relates to the way of evaluating delirium, which was assessed only once, daily and or every other day, not considering the possibility that the condition may fluctuate
throughout the day; therefore, it is possible that delirium was undersampled in some studies.

Identification of baseline frailty raises the possibility that it may be a potential therapeutic target in the prevention of delirium in the clinical practice. The results of this review may assist in encouraging early diagnosis of the frailty syndrome and delirium in the hospital setting, guiding prognosis, individualized care plans, and prevention of adverse outcomes.

Efforts should be directed towards mitigation and treatment strategies of delirium with early identification of risk factors\(^{[50]}\), in different clinical and surgical contexts.

Studies of the association between frailty and delirium in hospitalized older adults are still incipient, which highlights the need to investigate interventions for hospitalized older adults with frailty and delirium.

**Conclusion**

This study showed 34% prevalence of frailty and 21% of delirium in hospitalized older adults, with frailty being an independent risk factor for developing delirium, with an increased chance of 66% when compared to non-frail individuals.

**References**

1. Kashiwagi DT. Geriatric inpatient care: what should hospital clinicians know? Hospital Practice. 2020;48(1):1-2. https://doi.org/10.1080/21548331.2020.1723354
2. Morley JE, Vellas B, van Kan GA, Anker SD, Bauer JM, Bernabei R, et al. Frailty consensus: a call to action. J Am Med Dir Assoc. 2013;14(6):392-7. https://doi.org/10.1016/j.jamda.2013.03.022
3. Theou O, Squires E, Mallery K, Lee JS, Fay S, Goldstein J, et al. What do we know about frailty in the acute care setting? A scoping review. BMC Geriatrics. 2018;18(1). https://doi.org/10.1186/s12877-018-0823-2
4. Persico I, Cesari M, Morandi A, Haas J, Mazzola P, Zambon A, et al. Frailty and delirium in older adults: a systematic review and meta-analysis of the literature. J Am Geriatr Soc. 2018;66(10):2022-30. https://doi.org/10.1111/jgs.15503
5. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 5. ed. Washington, D.C.: American Psychiatric Publishing; 2013.
6. Marcantonio ER. Delirium in Hospitalized Older Adults. N Engl J Med. 2017;377:1456-66. https://doi.org/10.1056/NEJMcp1605501
7. Sillner AY, Holle CL, Rudolph JL. The overlap between falls and delirium in hospitalized older adults: a systematic review. Clin Geriatr Med. 2019;35(2):221-36. https://doi.org/10.1016/j.cger.2019.01.004
8. Morandi A, Di Santo SG, Zambon A, Mazzone A, Cherubini A, Mossello E, et al. Delirium, Dementia, and In-Hospital Mortality: The Results From the Italian Delirium Day 2016, A National Multicenter Study. J Gerontol Series A. 2019;74(6):910-6. https://doi.org/10.1093/gerona/gly154
9. Giroux M, Sirois MJ, Boucher V, Daoust R, Gouin É, Pelletier M, et al. Frailty Assessment to Help Predict Patients at Risk of Delirium When Consulting the Emergency Department. J Emerg Med. 2018;55(2):157-64. https://doi.org/10.1016/j.jemermed.2018.02.032
10. Bellelli PG, Biotto M, Morandi A, Meagher D, Cesari M, Mazzola P, et al. The relationship among frailty, delirium and attentional tests to detect delirium: a cohort study. Eur J Intern Med. 2019;70:33-8. https://doi.org/10.1016/j.ejim.2019.09.008
11. Pérez-Zepeda MU, Carrillo-Veja MF, Theou O, Jácome-Maldonado LD, García-Peña C. Hospital Complications and Frailty in Mexican Older Adults: An Emergency Care Cohort Analysis. Frontiers Med. 2020. https://doi.org/10.3389/fmed.2020.00505
12. Panza F, Solfrizzi V, Barulli MR, Santamato A, Seripa D, Pilotta A, et al. Cognitive frailty: A systematic review of epidemiological and neurobiological evidence of an age-related clinical condition. Rejuvenation Res. 2015;18(5):389-412. https://doi.org/10.1089/rej.2014.1637
13. Dani M, Owen LH, Jackson TA, Rockwood K, Sampson EL, Davis D. Delirium, Frailty, and Mortality: Interactions in a Prospective Study of Hospitalized Older People. J Gerontol A Biol Sci Med Sci. 2018;73(3):415-8. https://doi.org/10.1093/gerona/glx214
14. Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Chapter 5: Systematic reviews of prevalence and incidence. In: Aromataris E, Munn Z, editors. JBI Manual for Evidence Synthesis. Adelaide: JBI; 2020. https://doi.org/10.46658/JBIMES-20-06
15. Aromataris E, Munn Z, editors. JBI Manual for Evidence Synthesis. Adelaide: JBI; 2020. https://doi.org/10.46658/JBIMES-20-01
16. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. https://doi.org/10.1136/bmj.n71
17. Hulley SB, Cummings SR, Browner WS, Grady DG, Newman TB. Delineando pesquisa clinica. 4. ed. Apêndice 12A. Porto Alegre: Artmed; 2015.
18. R Core Team. R: A language and environment for statistical computing [Homepage]. Vienna: R Foundation for Statistical Computing; 2021 [cited 2022 Mar 21]. Available from: https://www.R-project.org/
19. Leung JM, Tsai TL, Sands LP. Brief report: preoperative frailty in older surgical patients is associated with early
postoperative delirium. Anesth Analg. 2011;112(5):1199-201. https://doi.org/10.1213/ANE.0b013e31820c7c06
20. Eeles EMP, White SV, O'Mahony SM, Bayer AJ, Hubbard RE. The impact of frailty and delirium on mortality in older inpatients. Age Ageing. 2012;41(3):412-6. https://doi.org/10.1093/ageing/afs021
21. Joosten E, Demuynck M, Detroyer E, Milisken K. Prevalence of frailty and its ability to predict in hospital delirium, falls, and 6-month mortality in hospitalized older patients. BMC Geriatr. 2014;14:1. https://doi.org/10.1186/1471-2318-14-1
22. Hempenius L, Slaets JP, van Asselt DZ, Schukking J, de Bock GH, Wiggers T, et al. Interventions to prevent postoperative delirium in elderly cancer patients should be targeted at those undergoing nonsuperficial surgery with special attention to the cognitive impaired patients. Eur J Surg Oncol. 2015;41(1):28-33. https://doi.org/10.1016/j.ejso.2014.04.006
23. Eide LSP, Ranhoff AH, Fridlund B, Haaverstad R, Hufthammer KO, Kuiper KJC, et al. Comparison of frequency, risk factors, and time course of postoperative delirium in octogenarians after transcatheter aortic valve implantation versus surgical aortic valve replacement. Am J Cardiol. 2015;115(6):802-9. https://doi.org/10.1016/j.amjcard.2014.12.043
24. Partridge JS, Fuller M, Harari D, Taylor PR, Martin FC, Dhesi JK. Frailty and poor functional status are common in arterial vascular surgical patients and affect postoperative outcomes. Int J Surg. 2015;18:57-63. https://doi.org/10.1016/j.ijsu.2015.04.037
25. Nguyen TN, Cumming RG, Hilmer SN. The Impact of Frailty on Mortality, Length of Stay and Re-hospitalisation in Older Patients with Atrial Fibrillation. Heart Lung Circ. 2016;25(6):551-7. https://doi.org/10.1016/j.hlc.2015.12.002
26. Assmann P, Kievit P, van der Wulp K, Verkroost M, Noyez L, Bor H, et al. Frailty is associated with delirium and mortality after transcatheter aortic valve implantation. Open Heart. 2016;3(2):e000478. https://doi.org/10.1136/openhrt-2016-000478
27. Chew J, Lim WS, Chong MS, Ding YY, Tay L. Impact of frailty and residual subsyndromal delirium in 1-year functional recovery: A prospective cohort study. Geriatr Gerontol Int. 2017;17(12):2472-8. https://doi.org/10.1111/ggi.13108
28. Ogawa M, Izawa KP, Satomi-Kobayashi S, Tsuboi Y, Komaki K, Gotake Y, et al. Impact of delirium on postoperative frailty and long term cardiovascular events after cardiac surgery. PLoS One. 2017;12(12):e0190359. https://doi.org/10.1371/journal.pone.0190359
29. Gleason LJ, Benton EA, Alvarez-Nebreda ML, Weaver MJ, Harris MB, Javedan H. FRAIL Questionnaire Screening Tool and Short-Term Outcomes in Geriatric Fracture Patients. J Am Med Dir Assoc. 2017 Dec 1;18(12):1082-6. https://doi.org/10.1016/j.jamda.2017.07.005
30. Tanaka S, Ueno M, Iida H, Kaibori M, Nomii T, Hirokawa F, et al. Preoperative assessment of frailty predicts age-related events after hepatic resection: a prospective multicenter study. J Hepatobiliary Pancreat Sci. 2018;25(8):377-87. https://doi.org/10.1002/jhp.568
31. Alabaf Sabbaghi S, De Souza D, Sarikonda P, Keevil VL, Wallis SJ, Romero-Ortuno R. Allocating patients to geriatric medicine wards in a tertiary university hospital in England: A service evaluation of the Specialist Advice for the Frail Elderly (SAFE) team. Aging Med (Milton). 2018;1(2):120-4. https://doi.org/10.1016/j.aggid.2018.01.001
32. Nomura Y, Nakano M, Bush B, Tian J, Yamaguchi A, Walston J, et al. Observational Study Examining the Association of Baseline Frailty and Postcardiac Surgery Delirium and Cognitive Change. Anesth Analg. 2019;129(2):507-14. https://doi.org/10.1213/ANE.000000000003967
33. Goudzwaard JA, de Ronde-Tillmans MJAG, El Faquir N, Acar F, Van Mieghem NM, Lenzen MJ, et al. The Erasmus Frailty Score is associated with delirium and 1-year mortality after Transcatheter Aortic Valve Implantation in older patients. The TAVI Care & Cure program. Int J Cardiol. 2019 Feb 1;276:48-52. https://doi.org/10.1016/j.ijcard.2018.10.093
34. Geriatric Medicine Research Collaborative. Delirium is prevalent in older hospital inpatients and associated with adverse outcomes: results of a prospective multicentre study on World Delirium Awareness Day. BMC Med. 2019;17(1):229. https://doi.org/10.1186/s12916-019-1458-7
35. Saravana-Bawan B, Warkentin LM, Rucker D, Carr F, Churchill TA, Khadaroo RG. Incidence and predictors of postoperative delirium in the older acute care surgery population: a prospective study. Can J Surg. 2019;62(1):33-8. https://doi.org/10.1503/cjs.016817
36. Goudzwaard JA, de Ronde-Tillmans MJAG, de Jager TAJ, Lenzen MJ, Nuis RJ, Van Mieghem NM, et al. Incidence, determinants and consequences of delirium in older patients after transcatheter aortic valve implantation. Age Ageing. 2020;49(3):389-94. https://doi.org/10.1093/ageing/afaa001
37. Itagaki A, Sakurada K, Matsuhama M, Yam JA, Yamashita T, Kohzuki M. Impact of frailty and mild cognitive impairment on delirium after cardiac surgery in older patients. J Cardiol. 2020;6(1):33-87. https://doi.org/10.1002/jhbp.568
38. Saljuqi AT, Hanna K, Asmar S, Tang A, Zeeshan M, Gries L, et al. Prospective Evaluation of Delirium in Geriatric Patients Undergoing Emergency General Surgery. J Am Coll Surg. 2020;230(5):758-65. https://doi.org/10.1016/j.jamcollsurg.2020.01.029
39. Susano MJ, Grasfield RH, Friese M, Rosner B, Crosby G, Bader AM, et al. Brief Preoperative Screening for Frailty and Cognitive Impairment Predicts Delirium after Spine Surgery. Anesthesiology. 2020;133(6):1184-91. https://doi.org/10.1097/ALN.0000000000003523
40. Mahanna-Gabrielli E, Zhang K, Sieber FE, Lin HM, Liu X, Sewell M, et al. Frailty Is Associated with Postoperative Delirium but Not With Postoperative Cognitive Decline in Older Noncardiac Surgery Patients. Anesth Analg. 2020;130(6):1516-23. https://doi.org/10.1213/ANE.000000000004773
41. Chen Y, Qin J. Modified Frailty Index Independently Predicts Postoperative Delirium and Delayed Neurocognitive Recovery After Elective Total Joint Arthroplasty. J Arthroplasty. 2021;36(2):449-53. https://doi.org/10.1016/j.arth.2020.07.074
42. Ministério da Saúde, Conselho Nacional de Saúde (BR). Resolução nº 510, de 7 de abril de 2016 [Internet]. Diário Oficial da União, 24 mai 2016 [cited 2022 Mar 21]. Available from: https://www.in.gov.br/materia/-/asset_publisher/Kujrw0TZC2Mb/content/id/22917581
43. Belleri G, Moresco R, Panina-Bordignon P, Arosio B, Gelfi C, Morandi A, et al. Is Delirium the Cognitive Harbinger of Frailty in Older Adults? A Review about the Existing Evidence. Front Med (Lausanne). 2017;4:188. https://doi.org/10.3389/fmed.2017.00188
44. Cesari M, Marzetti E, Thiem U, Pérez-Zepeda MU, Abellan Van Kan G, Landi F, et al. The geriatric management of frailty as paradigm of “The end of the disease era”. Eur J Intern Med. 2016 Jun;31:11-4. https://doi.org/10.1016/j.ejim.2016.03.005
45. Cunha AIL, Veronese N, Borges SM, Ricci NA. Frailty as a predictor of adverse outcomes in hospitalized older adults: A systematic review and meta-analysis. Ageing Res Rev. 2019;56:100960. https://doi.org/10.1016/j.arr.2019.100960
46. Lee JS, Auyeung TW, Leung J, Kwok T, Woo J. Transitions in frailty states among community-living older adults and their associated factors. J Am Med Dir Assoc. 2014;15(4):281-6. https://doi.org/10.1016/j.jamda.2013.12.002
47. Dent E, Morley JE, Cruz-Jentoft AJ, Woodhouse L, Rodríguez-Mañas L, Fried LP, et al. Physical Frailty: ICFSR International Clinical Practice Guidelines for Identification and Management. J Nutr Health Aging. 2019;23(9):771-87. https://doi.org/10.1007/s12603-019-1273-z
48. Abrahá I, Totta F, Rimland JM, Cruz-Jentoft A, Lozano-Montoya I, Soiza RL, et al. Efficacy of non-pharmacological interventions to prevent and treat delirium in older patients: a systematic overview. the senator project on top series. PLoS One. 2015;10(6):e0123090. https://doi.org/10.1371/journal.pone.0123090
49. Thomas C, Spank J, Weller S, Eschweiler GW. Nichtmedikamentöse Konzepte zu Prävention und Behandlung eines Delirs [Nonpharmaceutical concepts for prevention and treatment of delirium]. Z Gerontol Geriatr. 2021;54(8):759-67. https://doi.org/10.1007/s00391-021-01988-3
50. Siddiqi N, Cheater F, Collinson M, Farrin A, Forster A, George D, et al. The PiTSTOP study: a feasibility cluster randomized trial of delirium prevention in care homes for older people. Age Ageing. 2016 Sep;45(5):652-61. https://doi.org/10.1093/ageing/afw091

Authors’ contribution

Study concept and design: Clovis Cechinel, Maria Helena Lenardt, João Alberto Martins Rodrigues. Obtaining data: Clovis Cechinel, João Alberto Martins Rodrigues, Maria Angélica Binotto, Márcea Marrocos Aristides, Rosane Kraus. Data analysis and interpretation: Clovis Cechinel, Maria Helena Lenardt, João Alberto Martins Rodrigues, Maria Angélica Binotto, Márcea Marrocos Aristides, Rosane Kraus. Statistical analysis: Clovis Cechinel. Drafting the manuscript: Clovis Cechinel, Maria Helena Lenardt, João Alberto Martins Rodrigues, Maria Angélica Binotto, Márcea Marrocos Aristides, Rosane Kraus. Critical review of the manuscript as to its relevant intellectual content: Clovis Cechinel, Maria Helena Lenardt, Maria Angélica Binotto, Márcea Marrocos Aristides, Rosane Kraus. All authors approved the final version of the text.

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