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Predictors of outcomes of patients ≥ 80 years old admitted to intensive care units in Poland – a post-hoc analysis of the VIP2 prospective observational study

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Abstract

Background: Elderly patients pose a significant challenge to intensive care unit (ICU) clinicians. In this study we attempted to characterise the population of patients over 80 years old admitted to ICUs in Poland and identify associations between clinical features and short-term outcomes.

Methods: The study is a post-hoc analysis of the Polish cohort of the VIP2 European prospective observational study enrolling patients > 80 years old admitted to ICUs over a 6-month period. Data including clinical features, clinical frailty scale (CFS), geriatric scales, interventions within the ICU, and outcomes (30-day and ICU mortality and length of stay) were gathered. Univariate analyses comparing frail (CFS > 4) to non-frail patients and survivors to non-survivors were performed. Multivariable models with CFS, activities of daily living score (ADL), and the cognitive decline questionnaire IQCODE as predictors and ICU or 30-day mortality as outcomes were formed.

Results: A total of 371 patients from 27 ICUs were enrolled. Frail patients had significantly higher ICU (58% vs. 44.45%, $P = 0.03$) and 30-day (65.61% vs. 54.14%, $P = 0.01$) mortality compared to non-frail counterparts. The survivors had significantly lower SOFA score, CFS, ADL, and IQCODE than non-survivors. In multivariable analysis CFS (OR 1.15, 95% CI: 1.00–1.34) and SOFA score (OR 1.29, 95% CI: 1.19–1.41) were identified as significant predictors for ICU mortality; however, CFS was not a predictor for 30-day mortality ($P = 0.07$). No statistical significance was found for ADL, IQCODE, polypharmacy, or comorbidities.

Conclusions: We found a positive correlation between CFS and ICU mortality, which might point to the value of assessing the score for every patient admitted to the ICU. The older Polish ICU patients were characterised by higher mortality compared to the other European countries.

Key words: sepsis, intensive care, observational study, prospective study, multicentre study, frailty, geriatric population, mortality analysis, VIP study.

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Healthcare systems in developed countries are being increasingly challenged by issues associated with the aging society [1]. The global population of people 80 years of age or older is predicted to double by 2050 [2]. Care for older critically ill patients has been a topic of lively debate over the past decade. Recognising which patients would benefit from specialised care in the intensive care unit (ICU) is currently a major research topic and an essential component of quality critical care provision. Older ICU patients require a holistic assessment of their medical condition based on disorders highly prevalent in this population, such as frailty, dementia, delirium, or sarcopaenia [3].

Prognosis and outcomes of very old intensive care patients (VIPs) in Europe and several neighbouring countries have been investigated in the VIP1 cohort study in 2016/2017 [3, 4] and the VIP2 study [5] undertaken in 2018/2019 [3, 5]. Numerous Polish ICUs participated in both studies, and Poland contributed almost 10% of the data available in the VIP2 study. Compared to the first edition, the VIP2 study assessed additional variables, such as comorbidities, polypharmacy, or geriatric scale.

This hypothesis-generating study aimed to characterise the population of patients admitted to ICUs in Poland and explore relationships between clinical features and short-term outcomes, with special attention to frailty, comorbidities, polypharmacy, activities of daily living, and cognition.

METHODS

This study is a post-hoc analysis of a Polish sample of the Very Old Intensive Care Patients Study 2 (VIP2), which enrolled patients > 80 years old acutely admitted to intensive care units [6]. No specific exclusion criteria (apart from elective admissions) were introduced. The VIP2 study included patients admitted over 6 months between May 2018 and May 2019. The Polish subgroup was recruited from 27 Polish ICUs. The study's methodology has been described in detail in the original article [5].

Data regarding the patients' age, sex, reason for admission, pre-admission habitat, clinical frailty score (CFS), Sequential Organ Failure Assessment (SOFA) score within 24 hours of admission, length of stay in the ICU (LOS), 30-day and ICU survival, introduced procedures (non-invasive ventilation, intubation, vasopressors, renal replacement therapy), limitations of treatment, comorbidities, polypharmacy, the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), and the Activities in Daily Living (ADL) score was collected and analysed. Limitations of treatment were defined as either withdrawal of previously implemented life-sustaining treatment or withholding from escalating treatment. The comorbidities and polypharmacy were summarized additionally as comorbidity-polypharmacy score (CPS), a sum of several drugs taken by patients and their comorbidities.

Continuous variables were described with medians along with the interquartile range. The CFS score was analysed as a binary variable in univariate analysis comparing frail and non-frail patients, with CFS > 4 considered frailty, in par with a previous article summarising the Polish sample of VIP1 [4]. In logistic regression analysis, it was treated as a continuous variable, in accordance with the analysis in the main VIP2 study [5].

For univariate analysis, the Mann-Whitney test and χ^2 test were used for comparisons between frail and non-frail groups, as well as ICU survivor and non-survivor groups when applicable. Additionally, multiple regression analysis was performed to provide adjusted odds ratios (ORs) for variables of interest. To avoid multicollinearity, separate models for mortality were built with CFS, IQCODE, and ADL scores as predictors. The predictor variables were chosen to reflect the multivariable model formed in the main VIP study, with most baseline characteristics except for habitat being included in the model [5]. The patients with missing data points for multivariable analysis were excluded from the models.

In our study, a *P*-value of 0.05 was considered a statistical significance threshold.

RESULTS

A total of 371 patients (median age 84, IQR 81–87; 178 males) from 27 Polish ICUs (Table S1) were enrolled in the study (Table 1). 50.8% of the patients died in the ICU. Life-sustaining treatment was limited for 20.8% of patients.

Data on ICU survival was available for 364 patients (98.6%), and data on 30-day survival was available for 346 (93.3%) of the patients. Table S2 in the Supplementary Material presents the detailed data on missing values.

Frail vs. non-frail patients – univariate analysis

There were 53.9% frail patients in the sample. Frail patients were statistically significantly older than non-frail participants (85 vs. 83, $P < 0.01$), presented with more chronic comorbidities (5 vs. 4, $P < 0.01$), and took more drugs daily (6 vs. 5, $P = 0.03$). The ICU and 30-day mortality were significantly higher in the frail group compared to the non-frail group (Table 2).

Survivors vs. non-survivors – univariate analysis

The sample was almost evenly split between survivors and non-survivors, with 185 deceased and 179 survivors. The survivors had significantly lower SOFA score (8 vs. 11, $P < 0.01$), lower CFS (4 vs. 5, $P < 0.01$), lower ADL score (4 vs. 6, $P = 0.01$), and lower IQCODE score (3.5 vs. 3.8, $P = 0.03$) compared to the patients who died on the ICU. The length of stay of the survivors was significantly longer compared to the patients who died in the ICU (9.6 vs. 6.0, $P = 0.01$) (Table 3).

TABLE 1. Patient characteristics

Factor	
Number of patients	371
Sex (male), *n* (%)	178 (48.0)
Age (years)	84.00 (81–87)
Pre-admission habitat, *n* (%)	
Own home (including with spouse)	154 (41.5)
Other home with family or caregivers	85 (22.9)
Nursing home	7 (1.9)
Hospital ward	118 (31.8)
Other	2 (0.0)
SOFA score	10.00 (7–12)
CFS	5.00 (3.5–7.0)
IQCODE	3.7 (3.2–4.5)
ADL (Katz) score	5.0 (2.0–6.0)

SOFA – Sequential Organ Failure Assessment, CFS – Clinical Frailty Scale, IQCODE – Informant Questionnaire on Cognitive Decline of the Elderly, ADL – Activities of Daily Living

Multivariable analysis – CFS and geriatric scales

The multivariable analysis of ICU mortality identified CFS as an independent predictor of ICU mortality (OR 1.15, 95% CI: 1.00–1.34), along with SOFA score (OR 1.29, 95% CI: 1.19–1.41) (Table 4).

In a multivariable analysis including ADL (Katz scale), the questionnaire score was not identified as a significant predictor for patients' ICU mortality (OR 0.96, 95% CI: 0.84–1.11), with SOFA being once again the considerable predictor (OR 1.40, 95% CI: 1.26–1.57) (Table 5). Similar results were achieved for analysis with IQCODE, but it did not achieve statistical significance as a predictor of ICU mortality (OR 0.94, 95% CI: 0.59–1.48) (Table 6).

The data on the association between CFS, ADL, and IQCODE with 30-day mortality has beenis presented in the Supplementary material (Table S3–S5). None of the scales (CFS, ADL, IQCODE) was associated with 30-day mortality.

The number of comorbidities and drugs taken daily was not identified as a predictor of mortality in any of the models included in the analysis.

DISCUSSION

Our analysis of 371 elderly patients from 27 Polish ICU reaffirms some findings from the previous report of the Polish VIP1 cohort [4], again underlining

TABLE 2. Comparison of frail and non-frail patients. Frail defined as Clinical Frailty Scale > 4

Factor	All ($N = 371$)	Frail ($n = 200$)	Non-frail ($n = 171$)	*P*-value
Age (years)	84 (81–87)	85 (82.0–88.5)	83 (81–86)	< 0.01
Sex (male), *n* (%)	178 (48.0)	85 (42.5)	93 (54.3)	0.02
Number of chronic comorbidities	5 (3–7)	5 (4–7)	4 (2–6)	< 0.01
Number of drugs used	6 (4–8)	6 (5–8)	5 (3–8)	0.03
CPS	11 (8–15)	12 (9–15)	10 (6–14)	< 0.01
SOFA score	10.00 (7–12)	10.5 (8–13)	9 (7–11)	< 0.01
IQCODE score	3.7 (3.2–4.5)	4.3 (3.8–4.9)	3.3 (3.1–3.6)	< 0.01
ADL (Katz) score	5.0 (2.0–6.0)	3.0 (1.0–5.0)	6.0 (5.0–6.0)	< 0.01
Non-invasive ventilation, *n* (%)	29 (7.9)	19 (9.5)	10 (5.85)	0.20
Intubation and mechanical ventilation, *n* (%)	329 (88.9)	176 (88)	153 (89.47)	0.54
Vasoactive drugs usage, *n* (%)	325 (87.8)	174 (87.0)	152 (88.8)	0.59
Renal replacement therapy, *n* (%)	90 (24.5)	50 (25.0)	40 (23.7)	0.73
Limitations of treatment, *n* (%)	76 (20.8)	45 (22.5)	31 (18.1)	0.35
Length of stay on ICU (days)				
Survivors	5.10 (1.5–11.0)	7.7 (2.7–16.0)	6.1 (2.9–17.0)	0.94
Non-survivors	10.15 (3.98–22.83)	10.8 (4.9–18.9)	6.0 (3.0–16.5)	0.06
Overall ICU mortality, *n* (%)	185 (50.8)	58.00	44.45	0.01
30-day mortality, *n* (%)	203 (58.5)	65.61	54.14	0.03

CPS – Comorbidity-Polypharmacy Score, SOFA – Sequential Organ Failure Assessment, QCODE – Informant Questionnaire on Cognitive Decline of the Elderly, ADL – Activities of Daily Living, ICU – intensive care unit

TABLE 3. Comparison of ICU survivors and non-survivors

Factor	Survivors ($n = 179$)	Non-survivors ($n = 185$)	*P*-value
Age (years)	84 (81–87)	84 (82–87)	0.88
Sex (male), *n* (%)	90 (50.3)	89 (48.1)	0.41
Number of chronic comorbidities	5 (3–6)	5 (3–7)	0.76
Number of drugs used daily	6 (4–8)	6 (4–8)	0.51
CFS	4 (3–6)	5 (4–7)	< 0.01
CPS	11 (8–14)	11 (8–15)	0.794
SOFA score	8 (6–10)	11 (9–16)	< 0.01
IQCODE score	3.5 (3.2–4.3)	3.9 (3.3–4.7)	0.03
ADL score	6 (2.3–6.0)	4 (2–6)	0.01
Non-invasive ventilation, *n* (%)	18 (10.1)	11 (5.8)	0.21
Intubation and mechanical ventilation, *n* (%)	148 (82.7)	181 (94.6)	< 0.01
Vasoactive drugs usage, *n* (%)	145 (81.0)	175 (94.6)	< 0.01
Renal replacement therapy, *n* (%)	26 (14.5)	63 (34.0)	< 0.01
Limitations of treatment, *n* (%)	11 (6.1)	64 (31.9)	< 0.01
Length of stay on ICU (days)	9.6 (3.8–17.9)	6.0 (1.8–15.0)	0.01

CFS – Clinical Frailty Scale, CPS – Comorbidity-Polypharmacy Score, SOFA – Sequential Organ Failure Assessment, IQCODE – Informant Questionnaire on Cognitive Decline in the Elderly, ADL – Activities of Daily Living

CFS and SOFA as valuable predictors of patient mortality in the ICU. Furthermore, our results do not support the value of geriatrics scales (IQCODE, ADL) as well as the number of comorbidities and polypharmacy as predictors of outcomes for critically ill geriatric patients in the ICU.

Clinical Frailty Scale

Similarly to the Polish cohort of VIP1 and the main VIP2 study, our results identify a significant association between CFS and higher mortality. The impact of frailty on mortality was thoroughly assessed in VIP studies [3–5]. The usefulness of CFS

TABLE 4. The multivariable logistic regression model for ICU mortality – Clinical Frailty Scale. Number of observations $N = 363$

Characteristic	Estimate	Adjusted odds ratio (95% CI)	*P*-value
Intercept	–3.16		
Sex			
Male		Reference	
Female	0.11	1.12 (0.70–1.80)	0.64
Age	0.00	1.00 (0.94–1.06)	0.89
Admission reason			
Respiratory failure		Reference	
Circulatory failure	–0.33	0.72 (0.30–1.72)	0.46
Respiratory/circulatory failure	0.26	1.30 (0.63–2.69)	0.47
Sepsis	0.45	1.56 (0.71–3.48)	0.27
Trauma	0.99	2.69 (0.83–9.2)	0.10
Cerebral pathology	–0.55	0.58 (0.13–2.15)	0.43
Emergency surgery	0.23	1.25 (0.53–3.00)	0.61
Other	–0.34	0.71 (0.22–2.15)	0.56
SOFA score	0.26	1.29 (1.19–1.41)	< 0.01
CFS	0.14	1.16 (1.00–1.34)	0.05
Chronic comorbidities	0.05	1.05 (0.94–1.19)	0.37
Number of drugs taken daily	–0.02	0.98 (0.90–1.06)	0.60

SOFA – Sequential Organ Failure Assessment, CFS – Clinical Frailty Scale

TABLE 5. The multivariable logistic regression model for ICU mortality with ADL as predictor. Number of observations $N = 262$

Characteristic	Estimate	Adjusted odds ratio (95% CI)	*P*-value
Intercept	–10.0	–	–
Sex			
Male		Reference	Reference
Female	0.35	1.50 (0.78–2.9)	0.25
Age	0.8	1.09 (1.01–1.17)	0.04
Admission reason			
Respiratory failure	Reference	Reference	
Circulatory failure	–1.38	0.25 (0.05–0.84)	0.03
Respiratory/circulatory failure	0.03	1.15 (0.41–3.28)	0.95
Sepsis	0.10	1.11 (0.41–3.01)	0.84
Trauma	0.42	1.55 (0.35–6.84)	0.55
Cerebral pathology	–0.93	0.40 (0.04–2.40)	0.34
Emergency surgery	–0.39	0.41 (0.12–1.36)	0.46
Other	–0.82	0.77 (0.16–3.23)	0.25
Chronic comorbidities	–0.02	0.93 (0.81–1.08)	0.61
Number of drugs taken daily	0.02	1.04 (0.94–1.16))	0.65
ADL Score	–0.04	0.96 (0.82–1.12)	0.58

SOFA – Sequential Organ Failure Assessment, ADL – Activities of Daily Living

in predicting critical patients' mortality was found in the study of the whole VIP2 population [7, 8]. Utility of the CFS score was also stressed in the meta-analysis involving studies on critically ill patients with COVID-19 [9]. Our results further emphasise the importance of the CFS assessment for every elderly patient on admission because it is a simple and reliable prognosis tool.

SOFA score

We found a positive correlation between mortality and SOFA score. This finding is consistent with the re-

TABLE 6. The multivariable logistic regression model for ICU mortality with IQCODE included as predictor. Number of observations N = 243

Characteristic	Estimate	Adjusted odds ratio (95% CI)	*P*-value
Intercept	–11.9	–	–
Sex			
Male		Reference	Reference
Female	0.43	1.53 (0.83–2.87)	0.17
Age	0.10	1.11 (1.02–1.21)	0.01
Admission reason			
Respiratory failure		Reference	
Circulatory failure	–1.13	0.32 (0.87–1.11)	0.08
Respiratory/circulatory failure	0.09	1.18 (0.40–3.56)	0.86
Sepsis	0.32	1.37 (0.50–3.82)	0.54
Trauma	0.51	1.66 (0.41–6.89)	0.48
Cerebral pathology	–0.98	0.38 (0.05–2.07)	0.29
Emergency surgery	–0.60	0.55 (0.18–1.62)	0.28
Other	–0.76	0.47 (0.10–1.81)	0.29
SOFA score	0.31	1.37 (1.23–1.54)	< 0.01
Chronic comorbidities	0.00	1.00 (0.87–1.16)	0.96
Number of drugs daily	–0.01	0.99 (0.89–1.10)	0.91
IQCODE Score	–0.06	0.94 (0.59–1.48)	0.77

SOFA – Sequential Organ Failure Assessment, IQCODE – Informant Questionnaire on Cognitive Decline in the elderly

sults of the main VIP1 and VIP2 studies. The severity of organ dysfunction on admission is a well-documented predictor of outcomes [1, 3, 5, 10, 11]. Studies outside the VIP network also documented the predictive value of the SOFA score [10–12]. The SOFA score has been proposed as a triage tool to improve the allocation of critical care resources [12, 13].

Comorbidities and polypharmacy

The number of comorbidities or polypharmacy has not been validated as a valuable predictor of patient mortality in the literature or in our study. Several studies found an association between CPS and worse outcomes among patients [14]. One study of trauma victims aged 45 years or older found that CPS significantly correlated with higher mortality [15]. Another study of burn victims aged 45 years or more identified CPS as predictor of in-hospital complications but not mortality [16].

It is worth noting that the geriatric population differs from younger patients regarding patterns of comorbidities. Research in gerontology identifies several patterns of comorbidities and polypharmacy in elderly patients, with all profiles capable of achieving significant longevity [17]. Another issue is the ambiguity of polypharmacy as a predictor for negative outcomes on the ICU setting – there is no consensus on a clear threshold value of polypharmacy [18]. Consequently, the high number of comorbidities and polypharmacy might not predict the negative outcomes of elderly patients admitted to the ICU.

Geriatric scales: ADL, IQCODE

The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) is a 16-item screening tool for cognitive decline assessment [19, 20]. It was specifically developed to evaluate patients' cognitive abilities based only on information from caregivers. In our analysis it was associated with significantly higher mortality in univariate analysis, but in the multivariable model it was not identified as a significant predictor of ICU mortality. In the main VIP2 study IQCODE was not found to add new predictive value when added to frailty, but it was shown to impact 30-day survival; however, in the analysis of the main VIP2 study IQCODE was treated categorically, while in our analysis we applied it as a continuous value. It is worth noting that IQCODE was the variable with the highest number of missing values both in our sample (32.9% missing values) and in the general VIP2 population (24% of values missing). This might hint at difficulty in collecting the survey from the patients' caregivers [5].

The Activities of Daily Living (ADL) survey, also known as Katz score, is a simple 6-item survey of patients' independence in performing daily activities such as bathing or feeding [21]. The ADL score was not identified as an independent predictor of mortality in the ICU in the multivariable model. Similarly, although in the main VIP2 study it was associated with lower 30-day survival, it did not add any predictive value to the mortality model including frailty [5].

TABLE 7. Comparison of baseline data and outcomes between Polish cohort and the whole sample of VIP2

Factor	Polish sample ($n = 371$)	Whole VIP2 sample ($n = 3920$)
Sex (male), %	48.0	53.3
Age (years)	84 (81–87)	84 (81–87)
Pre-admission habitat, %		
Own home (including with spouse)	41.5	
Other home with family or caregivers	22.9	
Nursing home	1.9	73.811.15.49.20.9
Hospital ward	31.8	
Other	0	
SOFA score	10.00 (7–12)	6 (4–9)
CFS	5.00 (3.5–7.0)	4 (3–6)
IQCODE	3.7 (3.2–4.5)	3.19 (3–3.69)
ADL (Katz) score	5.0 (2.0–6.0)	6 (4.0–6.0)
Non-invasive ventilation, %	7.9	23.1
Intubation, %	88.9	49.9
Vasoactive drugs, %	87.8	59.5
Renal replacement therapy, %	24.5	11.0
Length of stay in the ICU (days)		
Non-survivors	5.10 (1.50–11.00)	3.67 (1.92–7.72)
Survivors	10.15 (3.98–22.83)	4.00 (1.54–8.46)
Death in the ICU, %	50.8	27.5
Death at 30 days, %	58.5	38.9
Life sustaining treatment limitation, %	20.8	34.0

SOFA – Sequential Organ Failure Assessment, CFS – Clinical Frailty Score, IQCODE – Informant Questionnaire on Cognitive Decline of the Elderly, ADL – Activities of Daily Living, ICU – intensive care unit

Similarly to IQCODE, there was a significant portion of missing values for ADL in our sample (27.5%).

Comparison of Polish ICUs to other countries

Polish VIPs had a markedly higher ICU and 30-day mortality compared to cohorts enrolled in the in the whole study sample (Table 7) or cohorts of other participating countries [8, 22]. The Polish cohort is also characterised by higher mortality and longer ICU LOS compared to participants of non-VIP studies on older ICU populations from France and Finland [5, 23]. Identifying reasons for such a difference in mortality and LOS between Poland and other countries is beyond the scope of this research. However, it is possible that Polish patients were admitted to the ICU later than in other countries and consequently were in a worse state on admission, which might be reflected in higher admission SOFA scores of Polish patients compared to the cohorts from the aforementioned studies. In fact, one article published in Intensive Care Medicine points out the fact that after adjusting for patients' condition on admission and number of beds, the standardised mortality ratio of Polish ICUs might be comparable to the ratios of Western countries [24]. That notion was supported by one of the post-hoc studies of the VIP2 project that found relatively low variance in ICU mortality between European countries when taking into consideration the standardised mortality ratio [25].

It is worth noting that it is no easy task for any clinician to decide about a patient's admission to the ICU and eventually find the optimal time for admission. According to a recent narrative review on the subject, no guidelines exist specifically for the critical care of patients over 80 years old. The guidelines for admission criteria to ICUs have been formed by the Polish Society of Anaesthesiology and Intensive Care, but they do not specifically cover the topic of the geriatric population [26, 27].

The prevalence of treatment limitations in Polish ICUs (20%) was noticeably lower compared to the whole VIP2 cohort as well as German and Norwegian cohorts [8, 28]. There is a significant variance in applying treatment limitations to elderly patients in ICUs across Europe. One study of COVID-19 patients identified a "North to South Gradient" in treatment limitations, with Northern European countries having the highest propensity to limit life-sustaining treatment and Southern European countries being characterised by the lowest rate of treatment limitations [29]. Numerous factors have been postulated as contribu-

tors to treatment limitation variability, including state legislation [30], religion [31], and cultural factors [31].

Limitations

The assessment of comorbidities and polypharmacy was simplified in the VIP2 study – we did not collect exact data on types of chronic conditions or drugs taken by patients. Our results could also be influenced by a limited group of patients and a high number of missing data in the assessment of geriatric scales – it is possible that due to the relatively low number of patients, the power of the multivariable models was insufficient. Due to the high number of conducted analyses, our results are prone to type I error and should therefore be interpreted with caution.

Strengths

The major strengths are the prospective design of the study and the participation of 27 ICUs from Poland. The sample included both academic and non-academic centres, increasing the generalisability of our results. The inclusion of new variables (particularly comorbidities, polypharmacy, and geriatric scales) allowed for a deepened analysis and assessment of the value of several clinical characteristics in predicting outcomes of critically ill patients.

CONCLUSIONS

Our study shows the value of assessing CFS for every older patient admitted to the ICU. The Polish cohort showed noticeably higher mortality and longer LOS compared with cohorts from other studies – the further studies might explore the reasons for such a discrepancy.

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