

Prevalence, clinical impact and associated patient-centred outcomes of advance directives in Swiss intensive care units: Results from the retrospective ADVISE Study

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Summary

STUDY AIMS: Data on the usefulness of advance directives for end-of-life decision-making in intensive care units (ICUs) are scarce. The primary aim of the present study was to investigate the prevalence of advance directives in patients of two Swiss ICUs. To contextualise how advance directives are created, interpreted and translated into clinical practice and which patient profiles influence whether and how patients choose to formulate advance directives, secondary objectives included analysing their content, clinical translation, and associated patient characteristics and outcomes.

METHODS: The retrospective cohort study was carried out at two tertiary Swiss ICUs. Data were collected from patients with advance directives treated in ICUs >48 hours from 2020 to 2022. The primary endpoint was the prevalence of advance directives and their content regarding life-prolonging measures, including cardiopulmonary resuscitation (CPR).

RESULTS: Of the 5242 patients included, 313 (6.0%) had advance directives. While 290/313 (92.7%) consented to life-prolonging measures other than CPR, CPR was less frequently desired (217/313 [69.3%]). 14.0% (18/129) requested CPR despite declining life-prolonging measures. Fewer women consented to life-prolonging measures and/or CPR than men, whereas prior ICU stays were associated with higher consent rates. Of 104 treatment adaptations, 53 (51.0%) aligned with advance directives, while 33/104 adaptations (31.7%) were based on presumed poor prognosis and 4/104 (3.9%) on surrogate decisions. While patients declining life-prolonging measures experienced faster treatment changes, survival and functional outcomes did not differ based on consent status.

CONCLUSIONS: The prevalence of patients with advance directives admitted to Swiss ICUs is low, and substantial obstacles must be overcome in clinical practice. Inconsistent or contradictory content highlights a need for better preemptive communication and documentation of patients' wishes. Respecting patient autonomy in choosing to forgo life-prolonging measures might not be associated with a lower likelihood of survival or functional outcomes.

Trial registration: <https://clinicaltrials.gov/NCT04348318>.

Introduction

Advance directives are legal instruments empowering individuals to specify healthcare preferences in case of incapacitation [1] (Swiss Academy of Medical Sciences: <https://www.samw.ch>). Despite their importance, the consistent use and screening for directives by healthcare professionals is insufficient. A review of 17 studies involving 149,413 patients and 1210 healthcare professionals found varying prevalence rates of advance directives in critically ill patients in intensive care units (ICUs), ranging from 2.6% in Northern and Southern Europe to 49% in North America, with consistently low screening rates (<10%) among healthcare providers [2]. When identified, advance directives are associated with increased do-not-resuscitate orders, care limitations, shorter ICU stays and reduced costs. However, challenges in implementing directives include inconsistent wording, variable adherence and complex patient preferences [2]. For instance, older adults in Switzerland have shown conflicting preferences, such as preferring cardiopulmonary resuscitation (CPR) while rejecting life-prolonging treatments such as mechanical ventilation [3]. These challenges result in physicians following directives by withholding resuscitation for up to 25% of patients [2]. While some studies suggest that advance di-

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rectives influence treatment decisions, evidence remains inconclusive and hampered by methodological issues [4–9]. Some studies suggest that patients with directives are less likely to receive life-sustaining treatments or die in hospitals [10–12], but a clear association with directives has yet to be demonstrated. A recent review reported that care adjustments are based on directives in 71% of cases in neurocritical ill adults [13]. However, the quality of evidence remains weak, with a high risk of bias [13].

Advance directives in elderly or frail patients may facilitate discussions with families, potentially enhancing ethical practices [14]. Limited evidence, however, suggests that directives influence ICU decisions on life-prolonging measures, with increased communication and ethical practices linked to better patient-centred outcomes [14]. The low prevalence of directives is concerning, and studies promoting their use and translation are lacking [13, 15]. The latter is critical as advances in modern intensive care medicine led to new and unforeseen situations with a substantial amount of patients surviving with severe disabilities [16–19]. Disabled ICU survivors, in addition, can be a significant psychological and economic burden for their relatives and families [16, 19]. Therefore, high-quality evidence regarding the use and translation of directives into clinical ICU practice is urgently needed.

Thus, given the evolving landscape of critical care and the increasing complexity of treatment decisions, the primary aim of the present study was to investigate the prevalence of advance directives regarding CPR and life-prolonging measures in ICU patients of two Swiss ICUs. To contextualise how advance directives are created, interpreted and translated into clinical practice and which patient profiles influence whether and how patients choose to formulate advance directives and what aspects they include, secondary objectives included analysing their content, clinical translation, and associated patient characteristics and clinical outcomes.

Methods

Design and ethics

This retrospective observational bicentric cohort study was performed at the ICUs of the Cantonal Hospital of Aarau and the University Hospital of Basel, both Swiss tertiary (academic) medical care centres. The ICU-specific characteristics of the two multidisciplinary ICUs during the study period were as follows:

In Aarau, the number of beds was between 20 and 30; the most frequent main diagnoses were cardiovascular, followed by gastrointestinal, metabolic, trauma, respiratory and neurological; the median NEMS (nine equivalents of nursing manpower use score) for the first 24 hours was 9 (interquartile range [IQR]: 1–18); the median length of stay was 0.9 days (0.6–1.9); and all-cause mortality was 3.1%.

In Basel, the number of beds was between 30 and 35; the most frequent main diagnoses were cardiovascular, followed by neurological, respiratory, gastrointestinal, metabolic and trauma; the median NEMS for the first 24 hours was 18 (IQR: 18–27); the median length of stay was 1.3 days (IQR: 0.9–2.6); and all-cause mortality was 6.1%.

The ethics committee of Northwest and Central Switzerland (<https://www.eknz.ch/>) approved the study (ID2020-00584), and the requirement for patient consent was waived. Data were collected for the ongoing bicentric ADVISE (Advance Directive Implementation and Scientific Evaluation) study (<https://clinicaltrials.gov> ID NCT04348318). STROBE guidelines were followed for study conduct, data acquisition, analysis and reporting [20]. Also, the study was conducted following the ethical principles laid down in the 1964 Declaration of Helsinki [21] and its later amendments. Information regarding the local Swiss jurisdiction can be obtained from the supplemental digital content in the appendix [22, 23].

Data collection

From January 2020 to December 2022 (deviating from the original study protocol and its amendments aiming to assess data from 2011 to 2022), the data of all consecutive adult patients (≥ 18 years) who were treated for ≥ 48 hours in ICUs of either centre were collected from the digital medical patient records and entered into a predefined online assessment interface within the database organiser REDCap version 14.1.2 (Research Electronic Data Capture) hosted by the University Hospital of Basel and developed by Vanderbilt University. REDCap is a secure, web-based software platform designed for data collection and management, featuring audit trails, user-level access controls and compliance with HIPAA and GDPR [24].

In addition to demographic data, the following clinical data were collected: ICU admission characteristics, principal diagnoses and severity of illness (as described in the following section) at ICU admission, level of consciousness at ICU admission, treatment characteristics, including non-invasive or mechanical ventilation, mechanical haemodynamic support, administration of vasopressors, antibiotics, opioids, artificial nutrition, blood products, and insertion of catheters and/or drains during intensive care. Patient records were further screened for notes regarding treatment adjustments during the ICU stay, including withdrawal/discontinuation of life-prolonging treatment and change of CPR status. The time elapsed from ICU admission to change of CPR status was noted. In addition, notes and discussions about withholding life-prolonging measures were assessed. Furthermore, we assessed inpatient outcomes, such as death and return to pre-morbid function at discharge and complications during ICU care, including infections and severe arterial hypotension requiring the use of vasopressors, as reported in patient records.

Quantification of illness severity

Illness severity was graded at admission to the ICU by using the Acute Physiology And Chronic Health Evaluation (APACHE) II score [25, 26], the Charlson Comorbidity Index [27] and the Good Outcome Following Attempted Resuscitation (GO-FAR) score [28, 29]. In brief, the GO-FAR score is a validated scoring system used in hospitalised patients to assess their likelihood of surviving a cardiac arrest with a good neurological outcome, defined as independent daily functioning with minimal to no disability [28, 29]. The score is based on various factors that can affect a patient's prognosis after a cardiac arrest, such as their age, underlying medical conditions and the initial rhythm

of their heart, with lower scores indicating a better chance of survival with a good neurological outcome [28].

Content of patients' written advance directives

The following aspects of the patients' advance directives were assessed and entered into the database:

- Date of directives and valid signature.
- Situations in which directives would be relevant.
- Directives regarding CPR.
- Directives regarding life-prolonging measures, including invasive mechanical ventilation, renal replacement therapy, mechanical haemodynamic support, artificial nutrition and surgery, but not including CPR.
- Agreements or disagreements with ICU and/or hospital admission.
- Best supportive care.
- Directives regarding hydration, pain management and administration of specific drugs, including anaesthetics, vasopressors, antibiotics, opioids and blood products.

Screening of all advance directives and data extraction were performed by four reviewers (SMB, PSCK, YE, DV), with continuous consultations to guarantee data robustness. In cases where interpretation of the directive content was unclear or ambiguous, RS (the study supervisor) was consulted. These cases were then discussed in a joint review process to reach consensus.

Primary and secondary endpoints

The primary endpoint was the prevalence of directives regarding CPR and life-prolonging measures in patients of two Swiss ICUs. Although detailed data analysis was limited to ICU patients with documented advance directives, we chose to report prevalence data relative to the entire ICU population during the study period. For the authors, this approach was justified by the current paucity of data on the use of advance directives in Swiss ICUs, making it essential to contextualise our findings by illustrating the overall frequency of advance directives in this setting.

Secondary endpoints were the clinical translation of directives, differences between patients consenting and not consenting to life-prolonging measures, their clinical characteristics, clinical translation, patient in-hospital outcomes including death, return to pre-morbid function and median GO-FAR scores. Clinical translation of directives was measured by treatment adaptations during intensive care, including withholding and/or withdrawal of life-sustaining measures, change of CPR status, time elapsed from ICU admission to treatment adaptations, and time elapsed from ICU admission to change of CPR status. These secondary endpoints were critical in contextualising how patients' directives are created, interpreted and translated into clinical practice and which patient profiles influence whether and how patients choose to formulate directives and what content they include.

Statistics

For descriptive statistics regarding baseline and admission characteristics and characteristics of the directives' clinical translation, continuous variables were summarised using

medians and interquartile ranges (IQRs). In contrast, categorical variables were summarised using counts and percentages. Further, patients were categorised as consenting or not to life-prolonging measures and consenting or not to CPR according to their directives. Among these groups, univariable comparisons of proportions were performed by the chi-squared test or Fisher's exact test. For comparisons of continuous variables, first the Shapiro-Wilk test was used to distinguish between normally and non-normally distributed variables. Second, normally distributed variables were analysed with the Student's t-test, whereas variables violating the normal distribution were analysed with the Mann-Whitney U test. The significance level for univariable comparisons of baseline and admission characteristics was adjusted using the Bonferroni correction for multiple comparisons and set at a significance level at a two-sided p-value ≤ 0.01 due to the Bonferroni correction.

Multivariable analyses were performed to identify characteristics independently associated with not consenting to life-prolonging measures and CPR using logistic regression, with significant associations being defined at a two-sided p-value ≤ 0.05 . Variables differing significantly in our univariable comparisons between patients consenting and not consenting to life-prolonging treatment or CPR were included in our multivariable models. As withdrawal/withholding of life-prolonging treatment due to presumed poor prognosis by the treating physicians may confound patients' consent to life-prolonging measures or CPR, we decided to include this variable into the multivariable models independent of its performance in the univariable comparisons. The Hosmer-Lemeshow chi-squared goodness-of-fit tests were performed for multivariable logistic regression models, which provide summary measures of calibration based upon a comparison of observed and estimated outcomes [30].

Statistical analysis was performed using Stata version 16.1 (StataCorp LLC, College Station, TX, USA).

No custom software libraries or unpublished code were used beyond built-in REDCap and Stata functionalities. The analytical workflow relied on standard Stata procedures, and no novel code was developed. As a result, no analytical code repository or DOI is available.

Results

Primary endpoints

Among 5242 ICU patients treated for ≥ 48 hours in the two ICUs (3160 in Basel; 2082 in Aarau), advance directives were retrospectively identified in 313 patients (6.0%; 245 in Basel; 68 in Aarau).

Secondary endpoints

Directives for life-prolonging measures and CPR

The proportion of patients with and without directives regarding life-prolonging treatment and CPR and the proportion of patients consenting and not consenting to these measures are presented in the flowchart (figure 1). Of the 313 patients with available advance directives, 290 (92.7%) provided directives regarding life-prolonging measures and 217 (69.3%) provided directives regarding

CPR. Of the 161 patients consenting to life-prolonging measures overall, 91 (56.5%) also consented to CPR. However, 18 of 129 patients not consenting to life-prolonging measures (14.0%) consented to CPR despite explicitly refusing life-prolonging measures and 26 of 117 patients consenting to CPR (22.2%) did not wish to receive life-prolonging measures (figure 1).

Baseline demographics and admission

86.3% of advance directives were completed using standardised templates, 91.4% designated a healthcare proxy and the median time between advance directive completion and ICU admission was two years (IQR: 0–4 years).

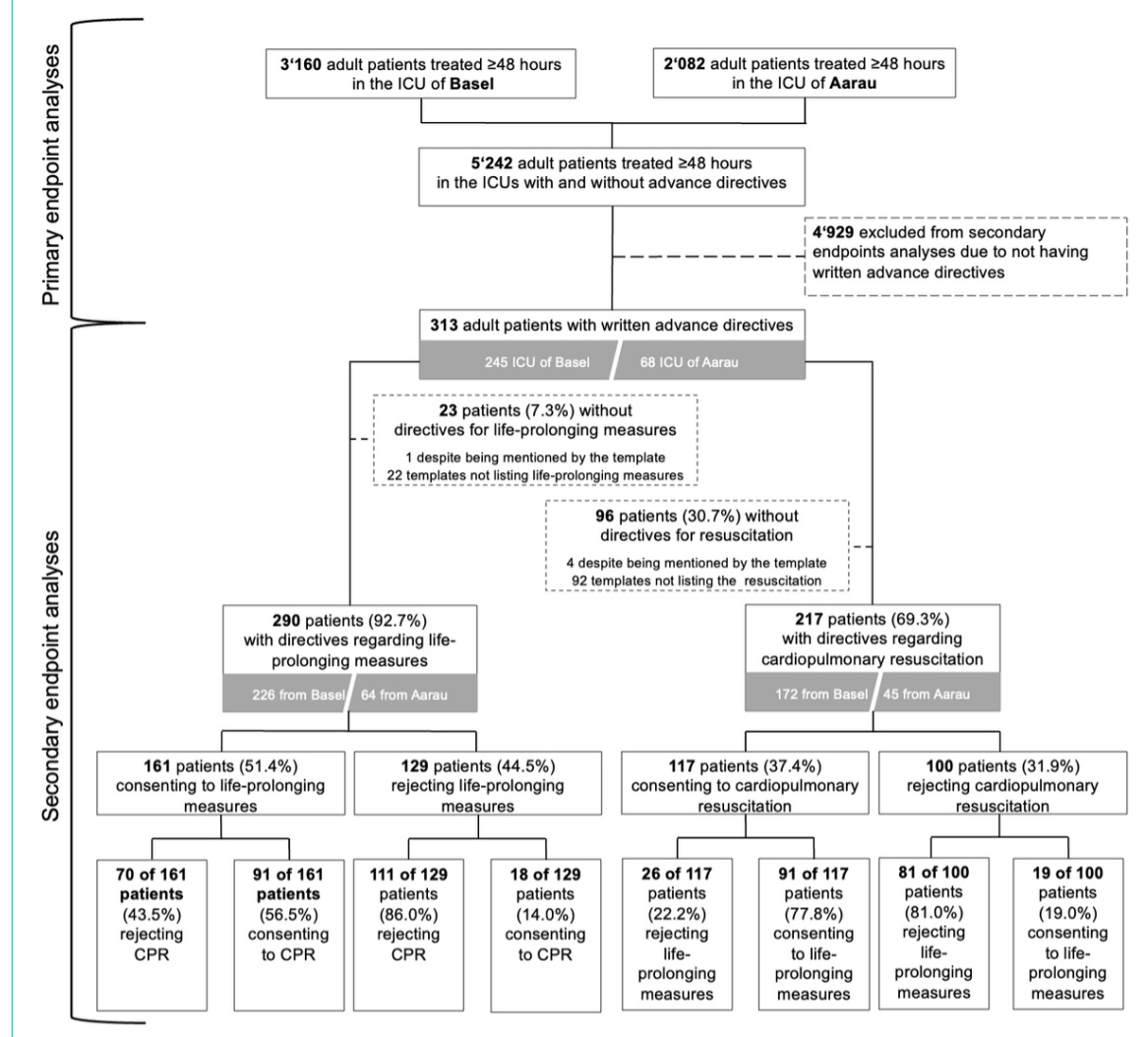
Appendix table S1 presents the demographics, clinical baseline and admission characteristics, and illness severity scores of all critically ill patients with written advance directives. Patients with advance directives were elderly (median age: 72 years, IQR: 65–79) and had a high burden of comorbidities (median Charlson Comorbidity Index: 5, IQR: 4–7). 131 patients (41.9%) were previously treated in intensive care units and 73 patients (23.3%) were care-dependent prior to hospital admission.

The median Glasgow Coma Scale (GCS) score at ICU admission was 8 (IQR: 3–14) and only 98 patients (31.3%) had a GCS ≥ 14 , indicating the potential ability to communicate their will independently. Thus, 215 (68.7%) had a lower GCS score, with 157 patients (48.6%) being comatose (GCS ≤ 8) at ICU admission.

Univariable comparisons of demographics and baseline characteristics between critically ill ICU patients consenting and not consenting to life-prolonging measures ($n = 290$) and cardiopulmonary resuscitation ($n = 217$) are presented in table 1 (upper half). Comparisons revealed that women declined life-prolonging measures more frequently than men despite having the same median age (72 years [IQR: 66–78] for men and 72 years [IQR: 65–78] for women). Patients previously treated in an ICU were more likely to consent to life-prolonging measures. Further comparisons revealed no differences regarding care dependency, civil status or confession after Bonferroni correction for multiple comparisons.

Univariable comparisons between patients consenting and not consenting to CPR ($n = 217$) revealed that patients not consenting to CPR were older and more frequently women (table 1, lower half).

Figure 1: Flowchart. CPR: cardiopulmonary resuscitation; ICU: intensive care unit. For the definition of life-prolonging measures, please refer to the Methods section.



Regarding CPR directives, no other differences in baseline or admission characteristics were identified between patients wanting and not wanting to be resuscitated after Bonferroni correction for multiple comparisons.

Table 2 presents multivariable models, including all demographic and clinical baseline characteristics significantly differing between patients consenting and not consenting to life-prolonging measures and CPR. These analyses revealed that female sex was independently associated with not consenting to life-prolonging measures and CPR.

Clinical translation of advance directives

Characteristics of the clinical translation and treatment adaptation of patients' advance directives among all patients (n = 313) are outlined in table 3, left columns.

Overall, treatment modifications documented in physician notes revealed that withdrawal/withholding of life-sustaining therapies and/or changes in CPR status occurred in over one-third of patients. The median time from ICU admission to treatment change was 3 days (IQR: 3–11) for CPR status and 6 days (IQR: 1–8) for other life-sustaining measures. Notably, 51.0% of treatment adaptations aligned with patients' directives, while 31.7% were based on presumed poor prognosis independent of directives or followed reasoning by surrogate decision-makers in 3.9% of cases. The reasons explicitly for withdrawal and/or withholding of life-sustaining measures and the change of CPR status revealed the same reasons with similar proportions as outlined in table 3.

Univariate analysis (n = 290) assessed the association between patient consent to life-prolonging measures and

Table 1:

Univariable comparisons of demographics and baseline characteristics between critically ill patients treated in the ICU for >48 hours and consenting and not consenting to life-prolonging measures (n = 290) and cardiopulmonary resuscitation (n = 217) according to their advance directives.

Characteristics	Patients consenting to life-prolonging measures (n=161)		Patients not consenting to life-prolonging measures (n=129)		p-value*
Demographics and baseline characteristics	n / median	% / IQR	n / median	% / IQR	
...Age (years; median, IQR)	71	65-78	72	67-80	0.109
...Female sex (n, %)	52	32.3	61	47.3	0.009
Baseline characteristics					
...Care dependency before admission (n, %)	39	24.2	30	23.3	0.847
...Previous ICU stay (n, %)	81	50.3	42	32.6	0.002
Civil status (n, %)					
...Married	82	50.9	57	44.2	0.836
...In partnership	12	7.5	13	10.1	
...Divorced	10	6.2	8	6.2	
...Single	4	2.5	2	1.6	
...Widowed	11	6.8	11	8.5	
...Unknown / Not stated	42	26.1	38	29.5	
Confession (n, %)					
...None	64	39.8	48	37.2	0.276
...Roman Catholic	46	28.6	34	26.4	
...Reformed	40	24.8	34	26.4	
...Other	4	2.5	10	7.8	
...Unknown / Not stated	7	4.4	3	2.3	
Characteristics	Patients consenting to CPR (n=117)		Patients not consenting to CPR (n=100)		p-value*
Demographics	n / median	% / IQR	n / median	% / IQR	
...Age (years; median, IQR)	69	62–77	75	68–82	<0.001
...Female sex (n, %)	35	29.9	52	52.0	0.001
Baseline characteristics					
...Care dependency before admission (n, %)	23	19.7	26	26.0	0.265
...Previous ICU stay (n, %)	51	43.6	36	36.0	0.255
Civil status (n, %)					
...Married	61	52.1	40	40.0	0.148
...In partnership	12	10.3	8	8.0	
...Divorced	8	6.8	5	5.0	
...Single	2	1.7	2	2.0	
...Widowed	6	5.1	14	14.0	
...Unknown / Not stated	28	23.9	31	31.0	
Confession (n, %)					
...None	50	42.7	43	43.0	0.038
...Roman Catholic	31	26.5	21	21.0	
...Reformed	27	23.1	26	26.0	
...Other	2	1.7	9	9.0	
...Unknown / Not stated	7	6.0	1	1.0	

CPR: cardiopulmonary resuscitation; ICU: intensive care unit; IQR: interquartile range.

* Statistical significance set at a two-sided p-value ≤0.009 after Bonferroni correction for multiple comparisons. Bolding indicates significance.

treatment adaptation according to documented directives as outlined in table 3, right columns. Analyses regarding the median time from ICU admission to CPR status change revealed that CPR status was changed sooner in patients not consenting to life-prolonging measures compared to those consenting.

Further details regarding withdrawal and withholding of specific life-sustaining measures among critically ill ICU patients consenting or not consenting to life-prolonging measures according to their advance directives (n = 290) are presented in appendix table S2. While the descriptive analyses revealed no differences regarding withdrawal or withholding of intensive care, CPR and treatment of infections, the number of patients not consenting to life-prolonging measures was higher regarding withdrawal or withholding of haemodynamic, respiratory and renal support, surgery, artificial nutrition and the administration of blood products.

Associated outcomes

In-hospital outcomes revealed no significant difference between patients consenting and not consenting to life-prolonging measures after the Bonferroni correction for multiple comparisons (table 3). Analyses regarding the median GO-FAR scores of survivors and non-survivors, as well as patients with and without return to premorbid baseline of critically ill patients with advance directives treated in the ICU for >48 hours consenting or not consenting to life-prolonging measures are shown in figures 2A and 2B. These analyses revealed no significant differences in median GO-FAR scores between survivors and non-survivors, regardless of their prior consent to life-prolonging measures. Similarly, surviving and non-surviving patients who did not consent to life-prolonging measures had comparable median GO-FAR scores.

In contrast, analyses of the GO-FAR scores for patients who consented to life-prolonging measures revealed higher scores in patients not reverting to their premorbid function (median score: 16 [IQR: 8–23] vs 11 [IQR: 1.5–17]; p = 0.007).

Discussion

This bicentric Swiss observational study investigated the prevalence, clinical translation and associated outcomes of advance directives in critically ill intensive care unit (ICU) patients. Our primary finding is that only 6% of patients

admitted for ≥48 hours had a documented advance directive, a concerning low proportion in a population at high risk of decisional incapacity. This low proportion of advance directives reinforces the urgent need for earlier and more widespread advance care planning, particularly as over two-thirds of patients with advance directives had a Glasgow Coma Scale (GCS) score <14 at ICU admission and were likely unable to express their will – underscoring the importance of preemptive documentation as previously discussed [2].

These results are consistent with previous studies, including a large prospective multicentre cohort involving 12,870 ICU patients across 199 ICUs in 36 countries, which reported an overall prevalence of advance directives of 13% in Central Europe, and even lower (3–4%) in Northern/Southern Europe, Asia, Latin America, Australia/New Zealand and Africa [14]. In Switzerland, national survey data estimate that only up to one-quarter of the population has a written advance directive, and only a minority are recognised upon hospital admission [3, 31]. The low prevalence of advance directives in our sample likely reflects this national reality, particularly among severely ill patients where decisional incapacity is common.

In contrast, the prevalence of advance directives in the US is higher, presumably due to the widespread use of central registries [14, 32]. In Switzerland, according to a national survey, only one-third of healthcare professionals are commonly involved in cardiopulmonary resuscitation (CPR), approximately two-thirds possess advance directives, two-thirds would refuse mechanical ventilation for themselves, and approximately 60% would not want to be resuscitated [33].

Content, consistency and interpretation of advance directives

Our analysis of the content of advance directives revealed substantial internal inconsistencies that suggest important challenges in patients’ understanding of intensive care and end-of-life decision-making. While 93% of patients with advance directives addressed life-prolonging treatments, only 69% specified preferences regarding CPR. Moreover, a notable proportion of patients expressed contradictory wishes, such as 14% of those declining life-prolonging treatments still requesting CPR, and 22% of CPR-consenting patients refusing other life-sustaining interventions. These findings are hypothesis-generating and suggest that, despite widespread use of standardised advance directive

Table 2: Uni- and multivariable analyses regarding characteristics associated with patients not consenting to life-prolonging measures and CPR.

Characteristics	Univariable analyses			Multivariable analyses		
Characteristics associated with not consenting to life-prolonging measures	uaOR	95% CI	p-value	aOR	95% CI	p-value*
...Female sex (vs male sex)	1.88	1.17–3.03	0.010	1.66	1.02–2.72	0.043
...Previous ICU stay (vs previous stay)	0.48	0.29–0.77	0.003	0.51	0.31–0.83	0.007
...Withdrawal/withholding life-prolonging measures due to presumed poor prognosis (vs no withdrawal/withholding)	0.28	0.11–0.70	0.007	0.31	0.12–0.79	0.015
Characteristics associated with not consenting to CPR	uaOR	95% CI	p-value	aOR	95% CI	p-value**
...Age (per increasing number of years)	1.04	1.01–0.06	0.008	1.04	1.01–1.06	0.008
...Female sex (vs male sex)	2.54	1.45–4.43	0.001	2.56	1.44–4.55	0.001
...Withdrawal/withholding life-prolonging measures due to presumed poor prognosis (vs no withdrawal/withholding)	0.41	0.17–1.04	0.060	0.41	0.16–1.05	0.062

aOR: adjusted odds ratio; CI: confidence interval; CPR: cardiopulmonary resuscitation; ICU: intensive care unit; uaOR: unadjusted odds ratio.

* Hosmer-Lemeshow goodness-of-fit test, chi-squared: 0.70; p = 0.706. Bolding indicates significance.

** Hosmer-Lemeshow goodness-of-fit test, chi-squared: 2.77; p = 0.948. Bolding indicates significance.

templates (86%) and healthcare proxy designations (91%), many patients may not fully grasp the medical implications of their decisions. This mirrors findings of the large prospective multicentre cohort work by Feldman et al. mentioned above [14], where patients frequently chose CPR but declined other interventions that would typically be part of post-resuscitation ICU care. Similar inconsistencies were also reported in a Swiss general population survey [3], in which many individuals who favoured CPR also rejected intubation and mechanical ventilation – despite the reality that CPR usually involves both.

These inconsistencies likely reflect misunderstandings about the goals and outcomes of intensive care and CPR,

as well as a potential overestimation of recovery potential from cardiac arrest [3]. They also point to structural limitations in the current advance directives templates, which may oversimplify complex clinical realities or fail to guide patients in articulating preferences that are internally coherent.

While these descriptive findings cannot establish causation, they provide a strong rationale for future prospective studies evaluating how educational interventions or guided discussions may improve the quality, clarity and consistency of advance directives. Another approach would be refining templates to improve clarity and facilitate physician adherence to patient wishes. In particular, adding a

Table 3:

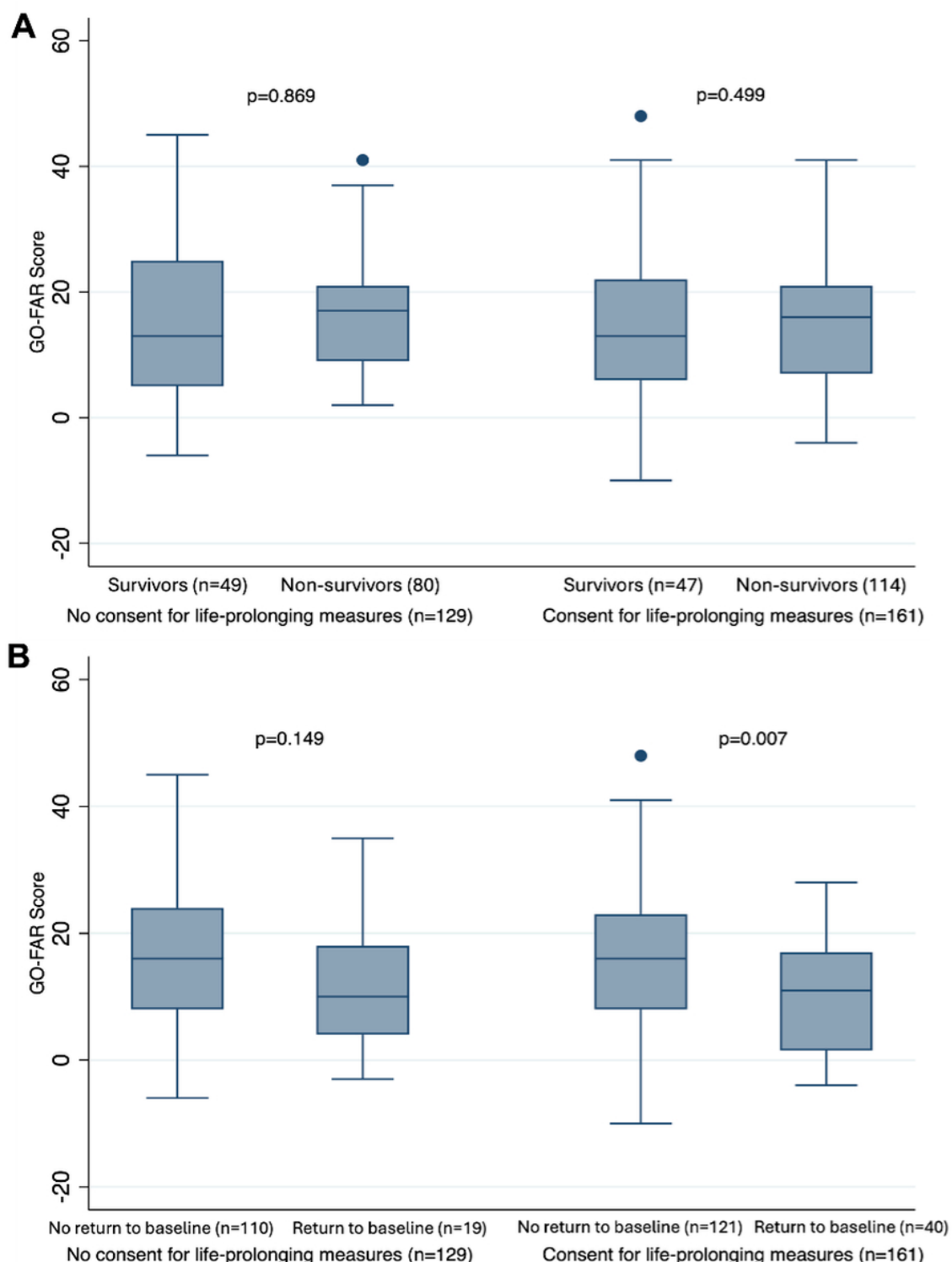
Characteristics of the clinical translation and treatment adaptation of patients' advance directives among all patients (n = 313) and their univariable comparisons between patients consenting and not consenting to life-prolonging measures (n = 290).

Characteristics	Patients with advance directives (total cohort n = 313, incl. 23 patients providing no information in this context)		Patients consenting to life-prolonging measures (n = 161)		Patients not consenting to life-prolonging measures (n = 129)		
Treatment adaptation during intensive care	n / median	% / IQR	n / median	% / IQR	n / median	% / IQR	p-value*
...Overall (not mutually exclusive; n, %)	104	33.2	52	32.3	42	32.6	0.963
.....Withholding of life-sustaining measures (n, %)	76	24.3	42	26.1	27	20.9	0.305
.....Withdrawal of life-sustaining measures (n, %)	63	20.1	35	21.7	22	17.1	0.318
.....Time from ICU admission to withdrawal of life-sustaining measures (days; median, IQR)	6	3–11	6	3–13	5	2–8	0.072
.....CPR status changed (n, %)	63	20.1	32	19.9	24	18.6	0.785
.....Time from ICU admission to CPR status change (days; median, IQR)	3	1–8	6	2–9	1	0–5	0.003
Noted reasons for treatment adaptation during intensive care (n, %)	n	% of sub-group	n	% of sub-group	n	% of sub-group	p-value*
...Of all patients with treatment adaptations (of 104 patients with treatment adaptations)	n	% of 104	n	% of 52	n	% of 42	
.....Translation of patients' directives	53	51.0	20	38.5	27	64.3	0.013
.....Presumed poor prognosis irrespective of directives	33	31.7	24	46.2	6	14.3	0.002
.....Treatment adaptation following reasoning of third parties (i.e., relatives, healthcare agents)	4	3.9	3	5.8	1	2.4	
.....No reasoning indicated in patient records	14	13.5	5	9.6	8	19.0	
...Reasons for withdrawal of life-sustaining measures of all patients (of 63 patients with withdrawal)	n	% of 63	n	% of 35	n	% of 22	
.....Translation of patients' directives	37	58.7	15	42.9	18	81.8	0.006
.....Presumed poor prognosis irrespective of directives	23	36.5	18	51.4	3	13.6	0.005
.....Treatment adaptation following reasoning of third parties (i.e. relatives, healthcare agents)	3	4.8	2	5.7	1	4.6	
.....No reasoning indicated in patient records	0	0.0	0	0.0	0	0.0	
...Reasons for withholding of life-sustaining measures (of 76 patients with treatment adaptations)	n	% of 76	n	% of 42	n	% of 27	
.....Translation of patients' directives	39	51.3	16	38.1	19	70.4	0.009
.....Presumed poor prognosis irrespective of directives	30	39.5	23	54.8	4	14.8	0.001
.....Treatment adaptation following reasoning of third parties (i.e. relatives, healthcare agents)	2	2.6	2	4.8	0	0.0	
.....No reasoning indicated in patient records	5	6.6	1	2.4	4	14.8	
...Reasons for CPR status change (of 63 patients with CPR status change)	n	% of 63	n	% of 32	n	% of 24	
.....Translation of patients' directives	31	49.2	12	37.5	16	66.7	0.031
.....Presumed poor prognosis irrespective of directives	21	33.3	16	50.0	2	8.3	0.001
.....Treatment adaptation following reasoning of third parties (i.e. relatives, healthcare agents)	0	0.0	0	0.0	0	0.0	
.....No reasoning indicated in patient records	11	17.5	4	12.5	6	25.0	
In-hospital outcomes							
...Length of intensive care unit stay (days; median, IQR)	6	3–11	6	4–11	5	3–9	0.240
...Length of hospital stay (days; median, IQR)	17	11–31	18	12–32	17	10–31	0.113
...In-hospital death (n, %)	104	33.2	47	29.2	49	38.0	0.114
...Return to premorbid function (n, %)	63	20.1	40	24.8	19	14.7	0.033

CPR: cardiopulmonary resuscitation; ICU: intensive care unit; IQR: interquartile range.

* Statistical significance set at a two-sided p-value ≤0.01 after the Bonferroni correction for multiple comparisons. Bolding indicates significance.

Figure 2: Median GO-FAR scores of (A) survivors and non-survivors as well as (B) patients with and without return to premorbid baseline of critically ill patients with advance directives treated in the ICU for >48 hours who consented or did not consent to life-prolonging measures. Box plot measures: centre line (box midline) represents the median GO-FAR score of each subgroup; box edges (top and bottom of the box) represent the 25th percentile (lower quartile) and 75th percentile (upper quartile) – this is the interquartile range (IQR); whiskers (extending from the box) to the smallest and largest values are within $1.5 \times$ IQR from the lower and upper quartiles, respectively. They capture the main range of the data; dots outside the whiskers represent outliers, i.e. individual patients with GO-FAR scores beyond $1.5 \times$ IQR from the box edges. GO-FAR: Good Outcome Following Attempted Resuscitation (range: -15 to 76) [41]. GO-FAR score and corresponding risk group (survival to discharge with minimal neurological disability*): GO-FAR score: ≥ 24 , very low survival (<1%); GO-FAR score: 14 to 23, low survival (1–3%); GO-FAR score: -5 to 13, average survival (3–15%); GO-FAR score: -15 to -6, above-average survival (>15%). * Patient is conscious, alert and able to work but might have mild neurological or psychological deficits, such as mild dysphagia or minor cranial nerve abnormalities [28].



section about the minimum quality of life acceptable for the individual to continue living might allow physicians to refrain from life-sustaining therapies when the probability of achieving the predefined minimum quality of life is minimal. As proposed in the “care planning umbrella model” by Hickman et al., caregivers, patients and relatives should decide together if a proposed treatment will result in the desired quality of life the patient has pre-specified [34]. Previous studies regarding interventions to increase the quality and recognition of advance directives revealed that the most effective approach is multimodal, using informative material and repeated conversations between healthcare professionals and patients [35].

Sex differences and prior ICU experience

Another hypothesis-generating finding in our study is the observed sex difference in treatment preferences. In our study, female sex was independently associated with declining both life-prolonging interventions and CPR, even after adjustment for age, comorbidities and previous ICU admission. This pattern is consistent with prior literature showing that women are more likely to limit intensive interventions [36] and that female sex is a risk factor for care limitation in the ICU [37, 38].

Our retrospective data cannot identify the underlying causes of this association, but potential explanations include sociocultural and generational influences, such as greater social isolation among elderly women or different perceptions of quality of life. These findings should be further explored in future studies using qualitative or prospective designs. Sociocultural factors may plausibly influence decision-making, especially among older cohorts. Women in these groups may face limited social support and isolation due to their longer life expectancy, often outliving their male counterparts. Additionally, men may still encounter more significant challenges in assuming caregiving responsibilities for their wives at home compared to the reverse. The latter, however, represents another hypothesis that deserves further attention in future studies.

Conversely, patients with prior ICU experience were more likely to consent to life-prolonging treatments. This may suggest that personal familiarity with intensive care fosters trust, rather than deterring patients from future ICU-level interventions. This finding, while exploratory, supports the idea that patient experience is a key factor influencing end-of-life preferences and may be valuable to address in advance care planning conversations.

Clinical translation of advance directives

Despite the relatively low prevalence and inconsistent content of advance directives, we observed that in 51.0% of cases, documented treatment adaptations aligned with the advance directives, while 31.7% were guided by presumed prognosis and 3.9% by surrogate decision-makers – proportions consistent with findings from the international study by Feldman et al. [14]. This suggests that advance directives, when available and interpretable, are often considered in clinical decision-making.

That said, treatment changes, including withdrawal or withholding of interventions and changes in CPR status, occurred early, typically within the first 3 to 6 days of

ICU admission, and CPR preferences were acted on more quickly when patients had declined life-prolonging measures. These patterns imply that clear directives may expedite decision-making, although the retrospective design limits causal inferences.

The variation in adherence to advance directives and reliance on surrogate decision-making further supports the need for more structured advance care planning that allows for interpretation aligned with patients' values and prognosis. Again, these are hypothesis-generating insights that require confirmation in prospective designs.

Associated outcomes

Importantly, no significant differences in in-hospital mortality or functional recovery were observed between patients consenting or not consenting to life-prolonging measures. This is a reassuring signal that respecting patient autonomy – even when it entails forgoing intensive interventions – does not necessarily compromise survival or recovery. These findings are, however, exploratory and limited by potential confounding and selection bias.

Among patients consenting to life-prolonging measures, those who failed to return to pre-morbid function had significantly higher GO-FAR scores, indicating a worse baseline prognosis (median 16 vs 11; $p = 0.007$). This difference may reflect that patients who are open to aggressive care sometimes carry an inherently higher risk of poor recovery. While these associations do not imply causality, they suggest a potential role for prognostic tools like GO-FAR to inform advance care planning and align expectations between patients and clinicians.

Limitations

The bicentric observational design limits the generalisability. However, many characteristics of our population are similar to those of other adult ICU cohort studies, such as age [39, 40], sex category [40], admission diagnosis [39] and illness severity [40]. Due to the retrospective nature of our study and inconsistent documentation in patient records, we could not attain comprehensive data regarding the exact time the treating healthcare professionals recognised directives. Therefore, we cannot exclude that patients for whom directives were recognised but not documented by the treating healthcare workers might have been missed. However, as the availability of advance directives is regarded as a significant advantage in patient-centred treatment, it seems unlikely that many such scenarios have not been documented. Another shortcoming of the retrospective design is the lack of proof that the decision to withdraw and/or withhold care was exclusively based on the patients' directives. Limited by the study's retrospective nature, we could not investigate the underlying reasons for the absence of patient directives. Hence, we could not distinguish between patients who never completed an advance directive and those for whom existing directives were not located or identified. As our study aimed to assess the prevalence of directives, this potential shortcoming did not affect our results.

Another confounder might be the fusion of the two separate ICUs into one at the medical care centre in Aarau in 2021 and concurrent team composition adaptations. The

retrospective design did not allow any assessments regarding the connection between the patients' quality of life and advance directives. However, the latter was not the aim of our study and could be overcome with future prospective studies. Lastly, the exclusion of patients without directives did not allow us to examine potential differences in patient characteristics between individuals with and without advance directives. The latter, however, was not the aim of the present study.

Conclusions

The prevalence of patients admitted to intensive care with advance directives is low, and substantial obstacles must be overcome to translate advance directives into clinical practice.

While the retrospective design limits causal conclusions, the hypothesis-generating findings of our secondary end-point analyses suggest that current advance directive practices may not fully support informed, value-based decision-making at the end of life. Our data reveal inconsistent or contradictory content of advance directives that highlight a need for better preemptive communication and documentation of patient wishes. Honouring patients' choices to refuse life-prolonging treatments does not seem to reduce their chances of survival or recovery. This highlights the ethical responsibility to improve advance care planning – by providing better systems, clearer tools and more effective education to support informed decision-making.

Data sharing statement

The datasets generated and analysed during the current study are not publicly available due to data protection regulations and institutional policy governing the use of sensitive patient information. However, deidentified study data (including associated data dictionaries) may be made available upon reasonable request to the principal investigator (RS), contingent upon approval by the corresponding institutional ethics committee and in compliance with applicable data privacy laws.

Requests must specify the intended use and type of analyses proposed. Data sharing will be limited to qualified researchers for purposes of scientific replication or secondary analyses that are aligned with the original research aims. Data access will be granted on a case-by-case basis under a formal data use agreement, and no data will be shared for commercial use.

Additional study documentation (e.g. study protocol, analysis code) may also be shared upon request where applicable. Data will remain available for such requests for a period of 5 years following publication of the study.

For all inquiries, please contact the principal investigator (i.e. corresponding author).

Acknowledgments

The corresponding author had full access to the complete dataset, and assumes responsibility for the integrity of the data and the accuracy of the data analysis.

Author contributions: Raoul Sutter, Sira M. Baumann, Dominik Vock and Simon A. Amacher planned and designed the study. Raoul Sutter, Sira M. Baumann, Paulina S.C. Kliem, Yasmin Erne and Simon A. Amacher acquired and interpreted the data. Raoul Sutter analysed the data and wrote the manuscript. Sira M. Baumann, Simon A.

Amacher, Yasmin Erne, Pascale Grzonka, Sebastian Berger, Sabina Hunziker, Martin Lohri, Caroline E. Gebhard, Mathias Nebiker, Luca Cioccarelli and Raoul Sutter interpreted the data, revised the manuscript and substantially contributed to the initial draft. All authors approved the final submitted version.

Use of artificial intelligence-assisted technologies: The grammar-checking software Grammarly (Grammarly, San Francisco, USA) was used to proofread and increase readability. The large language model ChatGPT-4o (OpenAI, San Francisco, USA) was used to paraphrase and summarise some of the manuscript's content. After using these applications, the authors edited the content as needed and verified its accuracy. The corresponding author takes full responsibility.

Potential competing interests

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Appendix

SUPPLEMENTAL METHODS

Local jurisdiction

In Switzerland, written advance directives (ADs) possess legal binding force according to the Swiss Society for Medical Sciences (SAMW) guidelines (21). However, several preconditions must be met:

- Decisional Capacity: The individual must demonstrably comprehend the content and consequences of decisions outlined in the directives.
- Formalities: The document requires the patient's signature or notarization for legal validity.
- Content: The content must comply with local laws and refrain from requesting illegal actions (e.g., euthanasia).

Physicians must adhere to the AD unless compelling reasons exist to believe it misrepresents the patient's current will or advocates for illegal actions.

Swiss advance directives serve two purposes:

1. Designation of a healthcare proxy, which acts as a surrogate decision-maker if the patient lacks decision-making capacity due to illness or trauma.
2. Legal document for the medical team outlining the treatment measures the patient wants to receive or the treatments he/she refuses.
 - The preferences regarding life-sustaining treatment measures, as outlined in the directive, overrule the preferences of the healthcare proxy or the medical team if the advance directive meets formal requirements. However, patients (or proxies) can't ask for non-beneficial treatments and/or interventions.
 - The proxies' decisions must be based on the patient's presumed wishes and best interests, following the written directives. This is decisive when the directives' specific wording is ambiguous.
 - Medical knowledge and expertise must be integrated into the shared decision-making process. This is particularly important if the directive is outdated, or the condition necessitates a different action. However, caregivers must consult the proxy (if defined) for shared decision-making in such specific situations.

The official Swiss Medical Association template for advance directives comprises two sections. First, patients express their general views on life and death. The second section prompts them to provide specific instructions regarding medical procedures and treatment objectives (22).

SUPPLEMENTAL TABLES

Supplemental Table 1: Baseline and admission characteristics of critically ill patients with advance directives treated in the ICU for >48 hours (n=313)

Characteristics	Patients with advance directives (n=313)	
Demographics and baseline characteristics	n / median	% / IQR
Age (years; median, IQR)	72	65-79
Female sex (n, %)	124	39.6
Care dependency prior admission (n, %)	73	23.3
Charlson Comorbidity Index (median, IQR)	5	4-7
Previous ICU stay (n, %)	131	41.9
Admission (n, %)		
Via paramedics	109	34.8
Patient (i.e., self-admission)	101	32.3
Via other hospital	72	23.0
Via practitioner	18	5.8
Via rehabilitation center	8	2.6
Via nursing home	5	1.6
Civil status (n, %)		
Married	146	46.7
In partnership	27	8.6
Divorced	22	7.0
Single	6	1.9
Widowed	87	27.8
Unknown / not stated	25	8.0
Confession (n, %)		
None	123	39.3
Roman catholic	84	26.8
Reformed	80	25.6
Others	15	4.8
Unknown / not stated	11	3.5
Illness severity scores (median, IQR)		
APACHE II (32 missing values)	29	24-35
GO-FAR	14	7-23
GCS at admission (median, IQR)	8	3-14
Initial principal diagnosis (not mutually exclusive; n, %)		
Postoperative care	49	15.6
Sepsis	40	12.8
Heart failure	28	9.0
Stroke	22	7.0
COVID-19	22	7.0
Pneumonia	16	5.1
Epileptic seizure	13	4.2
Myocardial infarction	12	3.8
Trauma	11	3.5
Chronic obstructive pulmonary disease exacerbation	10	3.2
Gastrointestinal bleeding	6	1.9
Acute liver failure	6	1.9
Delirium	4	1.3
Ketoacidosis	3	1.0
Encephalitis/Meningitis	3	1.0
Intoxication	2	0.6
Pulmonary embolism	1	0.3
Arrhythmia	1	0.3
Others	64	20.4
Availability and recognition of advance directives in the ICU (n, %)		
Directives available and recognized at ICU admission	239	76.4

Supplemental Table 1 continued.

Directives available and recognized later during ICU stay	74	23.6
Advance directives (n, %)		
Patients with directives regarding life-prolonging measures	290	92.7
Patients with directives regarding cardiopulmonary resuscitation	217	69.3

IQR = interquartile range; COVID-19 = Coronavirus disease 2019

APACHE II = Acute Physiology and Chronic Health Evaluation II (Range 0-71) (25,26); GO-FAR = Good Outcome Following Attempted Resuscitation (Range -15-76) (28, 41); Glasgow Coma Score (Range 3-15)

Supplemental Table 2: Comparisons of withdrawal and withholding of specific life-sustaining measures among critically ill patients treated in the ICU for >48 hours consenting or not consenting to life-prolonging measures according to their advance directives (n=290)

Withheld or withdrawn measures during intensive care	Patients consenting to life-prolonging measures (n=161)		Patients not consenting to life-prolonging measures (n=129)	
	n	%	n	%
Withdrawal of intensive care	28	17.4	23	17.8
CPR	24	14.9	18	14.0
Respiratory support (not mutually exclusive)	44	27.3	35	27.1
Intubation and mechanical ventilation	39	24.2	31	24.0
Escalation of respiratory support	20	12.4	17	13.2
Respiratory support with extracorporeal membrane oxygenation	6	3.7	14	10.9
Hemodynamic support (not mutually exclusive)	18	11.2	20	15.5
Hemodynamic support with vasopressors	15	9.3	15	11.6
Hemodynamic support with extracorporeal membrane oxygenation	6	3.7	14	10.9
Hemodynamic support with Impella	4	2.5	12	9.3
Hemodynamic support with left ventricular assist device	4	2.5	11	8.5
Renal support (not mutually exclusive)	9	5.6	15	11.6
Support with hemodialysis	8	5.0	15	11.6
Support with hemofiltration	5	3.1	12	9.3
Treatment of infections	17	10.6	14	10.9
Surgery	6	3.7	11	8.5
Artificial nutrition	16	9.9	16	12.4
Administration of blood products	6	3.7	7	5.4

Abbreviations: IQR = interquartile range; CPR = cardiopulmonary resuscitation; ICU = intensive care unit