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A randomized clinical trial to evaluate the effect of post-intensive care multidisciplinary consultations on mortality and the quality of life at 1 year

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Abstract

Purpose : Critical illness is associated with long-term increased mortality and impaired quality of life (QoL). We assessed whether multidisciplinary consultations would improve outcome at 12 months (M12) after intensive care unit (ICU) discharge.

Methods : We performed an open, multicenter, parallel-group, randomized clinical trial. Eligible are patients discharged alive from ICU in 11 French hospitals between 2012 and 2018. The intervention group had a multidisciplinary face-to-face consultation involving an intensivist, a psychologist, and a social worker at ICU discharge and then at M3 and M6 (optional). The control group had standard post-ICU follow-up. A consultation was scheduled at M12 for all patients. The QoL was assessed using the EuroQol-5 Dimensions-5 Level (Euro-QoL-5D-5L) which includes five dimensions (mobility, self-care, usual activities, pain, and anxiety/depression), each ranging from 1 to 5 (1: no, 2: slight, 3: moderate, 4: severe, and 5: extreme problems). The primary endpoint was poor clinical outcome defined as death or severe-to-extreme impairment of at least one EuroQoL-5D-5L dimension at M12. The information was collected by a blinded investigator by phone. Secondary outcomes were functional, psychological, and cognitive status at M12 consultation.

Results : 540 patients were included (standard, $n=272$; multidisciplinary, $n=268$). The risk for a poor outcome was significantly greater in the multidisciplinary group than in the standard group [adjusted odds ratio 1.49 (95% confidence interval, (1.04–2.13)]. Seventy-two (13.3%) patients died at M12 (standard, $n=32$; multidisciplinary, $n=40$). The functional, psychological, and cognitive scores at M12 did not statistically differ between groups.

Conclusions : A hospital-based, face-to-face, intensivist-led multidisciplinary consultation at ICU discharge then at 3 and 6 months was associated with poor outcome 1 year after ICU.

Keywords: Critical illness, Post-ICU syndrome, Quality of life, Mortality

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Introduction

Critical illness is associated with long-term mortality and impaired quality of life (QoL) [1], of which ranges from 29% to 60% [1–4] after discharge from intensive care unit (ICU). These rates differ depending on the patient's age, medical history, critical illness severity, and ICU care [1]. This poor outcome appears to be mainly the consequence of various post-ICU disorders affecting the physical abilities, psychological status, and cognitive functions. Physical disabilities are reported in 14–39% of patients at 1 year after ICU discharge, and are mostly related to ICU-acquired weakness [5–8]. Post-ICU psychological disorders affect 20–70% of the patients [8–11], and include anxiety, depression, and post-traumatic stress syndrome (PTSD) [12]. Thirty-to-ninety percent of patients complain from impaired memory, focus, and concentration [13–17]. These post-ICU disorders have a major impact on surviving and QoL. They are also associated with re-hospitalization [18–20], and decreased return to home and work [21]. In addition, post-ICU disorders and patients' socio-economic status have a reciprocal impact on each other [22]. Therefore, it can be inferred that the alleviation of post-ICU disorders will result in both improved surviving and QoL. No randomized clinical trial (RCT) has shown that a post-ICU intervention could improve the surviving and QoL after ICU [18, 23–28]. We tested the hypothesis that a joint consultation involving medical, psychological, and social management could be more appropriate to target the main dimensions and consequences of post-ICU disorders.

Therefore, we conducted the SUIVI-REA (FOLLOW-UP ICU) trial to assess the impact of a multidisciplinary consultations on death and QoL at 1 year after ICU discharge. The secondary objectives included the impact of these appointments on physical, psychological, cognitive, and social status, as well as medical referrals.

Methods

Study design

SUIVI-REA was an open, multicenter, parallel-group RCT conducted in 11 French ICUs. It aimed to compare multidisciplinary consultations to standard follow-up among patients discharged alive from ICU. The overall duration of the study was 1 year for each participant [29]. Ethics approval was granted by the French regulatory board (Comité de Protection des Personnes of Saint-Germain en Laye, France), on 08/07/2011. The trial was registered on ClinicalTrials.gov (NCT01796509). Written informed consent was obtained from all patients.

Take-home message

Our study shows that a hospital-based, face-to-face, intensivist-led multidisciplinary consultation, involving an physiscian from the intensive care unit (ICU), a psychologist and a social worker and provided at ICU discharge then at 3 month and 6 months (optional), deteriorates the quality of life at 12 months, in comparison to standard post-ICU follow-up. These results appear similar to previous studies which showed no or limited benefit of this intervention. This study further shows that the anxiety/depression domain of the quality of life is significantly impacted by ICU and that the intervention failed to improve the functional, psychological, and cognitive status at 1 year.

Eligibility criteria

Adult patients were eligible if they lived within 100 km from the participating center, received mechanical ventilation (MV) for more than 3 days; had a life expectancy greater than 1 year (defined by a McCabe score < 2 and the absence of metastatic cancer); had a general practitioner (GP); were affiliated to the national health insurance system; provided written informed consent. The initial exclusion criteria were: hospitalization in an ICU in the previous year; pre-existing chronic myopathy, psychiatric disorder or dementia; ICU admission for serious burns, severe brain injury, suicide or self-induced poisoning; patients under legal guardianship, not fluent in French, homeless or pregnant. The exclusion criteria were amended to improve patient recruitment by allowing the enrollment of patients admitted to ICU for coma, Guillain–Barré syndrome, voluntary drug poisoning, or multiple trauma without serious head trauma but also patients who were confused when leaving the ICU (if their relative consented).

Randomization and interventions

Eligible patients were randomly assigned in a 1:1 ratio to receive either post-ICU "multidisciplinary consultations" or "standard follow-up". The randomization was stratified by center using a permuted block of unrevealed size randomization and a central, concealed, web-based, automated randomization system (electronic supplementary material, ESM).

Patients were included at time of ICU discharge. In both groups, medical, psychological, and social data were collected at time of inclusion. The Sequential Organ Failure Assessment (SOFA) score was collected at ICU admission. Patients were asked to retrospectively score their QoL 3 months before ICU and at inclusion, using the Euro Quality of Life-5 dimensions and 5 levels questionnaire (EQ5D-5L).

The EQ5D-5L includes five dimensions (i.e., mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each of which has five levels of response (1:

no problems, 2: slight problems, 3: moderate problems, 4: severe problems, and 5: extreme problems/unable to). The EQ5D-5L is based on a visual analogue scale (VAS) which permits the patient to rate his/her perceived health from 0 (the worst imaginable health) to 100 (the best imaginable health). Finally, an EQ5D-index can be calculated, using country value sets. It ranges from ≤ 0 (bad health with death = 0), to 1 (good health). It should be noted that the calculation was not initially planned as there was no French population-based evaluation studies at the time of our study conception [30].

Patients allocated to the "standard" group had a single post-ICU consultation at 12 months (M12). Patients allocated to the "multidisciplinary" group had a consultation at time of ICU discharge, at 3 months (M3), at 6 months (M6) if found necessary and finally at M12 after ICU discharge. For both groups, the M12 consultation was scheduled after collection of the primary endpoint.

In both groups, these planned consultations involved an ICU physician, a psychologist, and a social worker (see ESM). The ICU physician consultations included: (1) collection of the current treatment, weight, vital signs, comorbidities, and symptoms; (2) date, of re-admission at the hospital, if any; (3) standardized general examination; (4) assessment of functional status using the Medical Research Council (MRC) sum score for assessing muscle strength, Barthel's index and the Instrumental Activities of Daily Living (IADL) score for assessing disability; (5) assessment of cognitive status using the Minimal Mental State Examination (MMSE). The ICU physician could prescribe paraclinical explorations or treatment, but it was recommended that they refer to the patient's GP, except in the case of an emergency.

The psychologist conducted an interview during which the participant reported any psychological difficulties. We also used the Hospital Anxiety and Depression scale (HADS) and the Impact Event Scale-Revised (IES-R) to assess PTSD. Consultation with the social worker consisted of a social questionnaire and an interview to collect EQ5D-5L items (except at M12 to respect the blinded outcome assessment), as well as social and professional issues and needs. Then, the multidisciplinary team met to discuss the participant's status and requirements. A summary report was sent to the patient's GP but not to the patient directly, as originally planned.

To improve patients' adherence, the research assistant of each center organized the consultations and patients were reminded of these consultations by mail two weeks prior.

Outcomes and assessment

The primary endpoint was poor outcome defined by death or severe (i.e., score 4/5) to extreme (i.e., score 5/5) impairment of at least one dimension of the EQ5D-5L at 12 months. The EQ5D-5L and EQ-VAS were collected by phone by the same blinded investigator. Indeed, the latter was a research assistant specifically trained for this task who was not involved in the organization of the post-ICU consultations and was not informed by the patient of his assignment. He completed 92% of the EQ5D-5L at M12 directly with the patient himself on the phone (Table S1, ESM). Neither the participants nor the investigators (i.e., ICU physicians, psychologists, and social workers) were blinded for the patient's assignment to one of the trial groups. The EQ5D-index score was calculated.

We opted for a combined primary endpoint because: (1) death and impaired QoL are two long-term consequences of post-ICU disorders; (2) poor QoL is associated with higher mortality [31], indicating that deceased patients likely had poor QoL before; (3) the alleviation of post-ICU disorders could then improve surviving and QoL. As mentioned above, death is built into the EQ5D-index score, indicating that death was considered a poor QoL.

The secondary outcomes were collected at M12 consultation and included cognitive (i.e., MMS), psychological (i.e., HADS and IES-R), and functional status (i.e., MRC-sum score, Barthel index, and IADL), return to home and return to work, as well as the number of re-hospitalization and outpatient consultations within these 12 months. Compliance with multidisciplinary recommendations and patients' satisfaction were assessed at M12.

Statistical analysis

At the time of the study design, other studies reported that 50% patients discharged from ICU had an unfavorable outcome at M12, including death (10%) or severe impairment on at least one dimension of the EQ5D-5L (40%) [24, 32]. This study was powered to detect a decrease from 50 to 37% of patients with unfavorable outcome with a power of 80% and a two-sided 5% alpha risk. Accordingly, the estimated sample size was 498 patients (249 per group). It was increased to 600 patients, based on an attrition rate of 20%. Because the attrition rate was half the one expected, an amendment allowed us to reduce the sample size to 520. Finally, 546 patients have been included.

Data were analyzed using R version 4.1.1 (2021–08-10, R Foundation for Statistical Computing).

Baseline characteristics are described overall and by group. Quantitative variables are described as median

[first quartile (Q1) and third quartile (Q3)], and qualitative variables as number and percentage.

The main analysis of the primary outcome was by intention to treat (ITT) using a logistic regression model. The adjustments were based on the center as a fixed event and the main risk factors for post-ICU disorders: age at ICU entrance (≤ or > 65 yo) and severity of critical illness (according to SOFA score upon admission) [22, 33]. Missing values for QoL dimensions at M12 were completed using a multiple imputations method. The missing data mechanism was assessed by comparing the baseline characteristics of the responders and non-responders and was presumed to be a missing at random mechanism. Ten imputations were done, with 100 iterations each. The pooled data of the 10 imputations were used to model the relationship between variables (ESM).

Three other analyses of the primary outcome were considered as sensitivity analyses: (i) a worst-case and a best-case scenario analysis using a logistic regression model, (ii) a complete case analysis on the primary outcome using a logistic regression model [modified ITT (1)], and (iii) a multinomial model where the missing outcome was considered as a third category [modified ITT (2)] (see ESM).

Secondary outcomes were compared using Student's test in case of normal distribution. Otherwise, the Wilcoxon test was used for quantitative variables and the chi-squared test (or Fisher's exact test as appropriate) for qualitative variables. No imputation was performed on secondary outcomes.

It should be noted that the sample size was calculated to conclude exclusively on the primary endpoint. All secondary analyses are exploratory analyses which provide a trend and not a causal relationship between secondary outcomes and the randomization group. All reported p values were not adjusted for multiple testing. The statistical analysis plan was written and validated in March 2022. The database was freezed on May 2022.

Results

A total of 546 patients were randomized between 20 December 2012 and 1 September 2017, of whom 6 withdrew their consent, resulting in 540 included in the main analysis. Among those 272 (50.4%) were randomized to the "standard" and 268 (49.6%) to the "multidisciplinary" group (Fig. 1). Baseline characteristics were well balanced between groups (Table 1).

Multidisciplinary consultations

Among the 268 patients included in the multidisciplinary group, 202 (75.4%) attended the first multidisciplinary consultation before ICU discharge, considering 2 (0.7%) died and 64 (23.9%) were discharged before the first consultation could have been set up.

Only 241/268 (89.9%) were noticed to attend the M3 consultation (Table 2). Among them, 155 (64.3%) accepted and 86 (35.7%) refused to attend (Table 2). Asthenia, dyspnea, motor, and sensory deficits were the most frequent symptoms (Table 2). A fifth to a quarter of patients were recommended to consult a physician, a psychologist (or a psychiatrist) or a social worker (Table 2). Patients who attended M3 consultations had better QoL "3 months before ICU", shorter length of ICU stay and tended to have better functional status but worse psychological status at baseline (Table S2, see ESM). In the multidisciplinary group, 267 (99.6%), 161 (60.1%), and 21 (7.8%) patients attended one, two, and three multidisciplinary consultations.

Primary outcome

Among the 540 randomized patients, 43 (8%) had a missing QoL at M12 (Fig. 1 and Table S3, see ESM). 226 patients/497 (45.5%) had a poor outcome at M12, including 104/252 (41.2%) and 122/245 (49.7%), in the standard and multidisciplinary groups, respectively. 72 (13.3%) patients died within follow-up period, including 32 (44%) in the standard and 40 (56%) in the multidisciplinary group (Table S4, ESM).

In the main ITT analysis (adjusted for center, age, and SOFA), the risk of bad outcome at M12 was significantly higher in the multidisciplinary group (adjusted odds ratio (OR) = 1.49 [95% confidence interval (CI) 1.04–2.13]) (Table 3).

In contrast to the best-case scenario model (adjusted OR = 1.03 [95% CI 0.73–1.47]), the worst-case scenario analysis, the per-protocol, and the two modified ITT adjusted models showed that the multidisciplinary consultations were significantly associated with poor outcome (Table S5, ESM). This statistical relationship was maintained after adjustment for QoL "3 months before ICU" and most relevant baseline characteristics (adjusted OR = 1.46 [95% CI 1.01–2.12]) (Tables S6–S7, ESM). It was also confirmed when the primary outcome was defined as "death or moderate-to-extreme impairment in at least one EQ5D dimension" (adjusted OR = 1.61 (95% CI 1.09–2.40]) (Tables S8–S10, ESM).

Secondary outcomes

Among the EQ5D-5L dimensions (excluding missing values and deaths), only the psychological dimension differed between groups, with a higher proportion of patients with anxiety or depression at M12 in the multidisciplinary group (Figs. 2 and supplementary S1). The

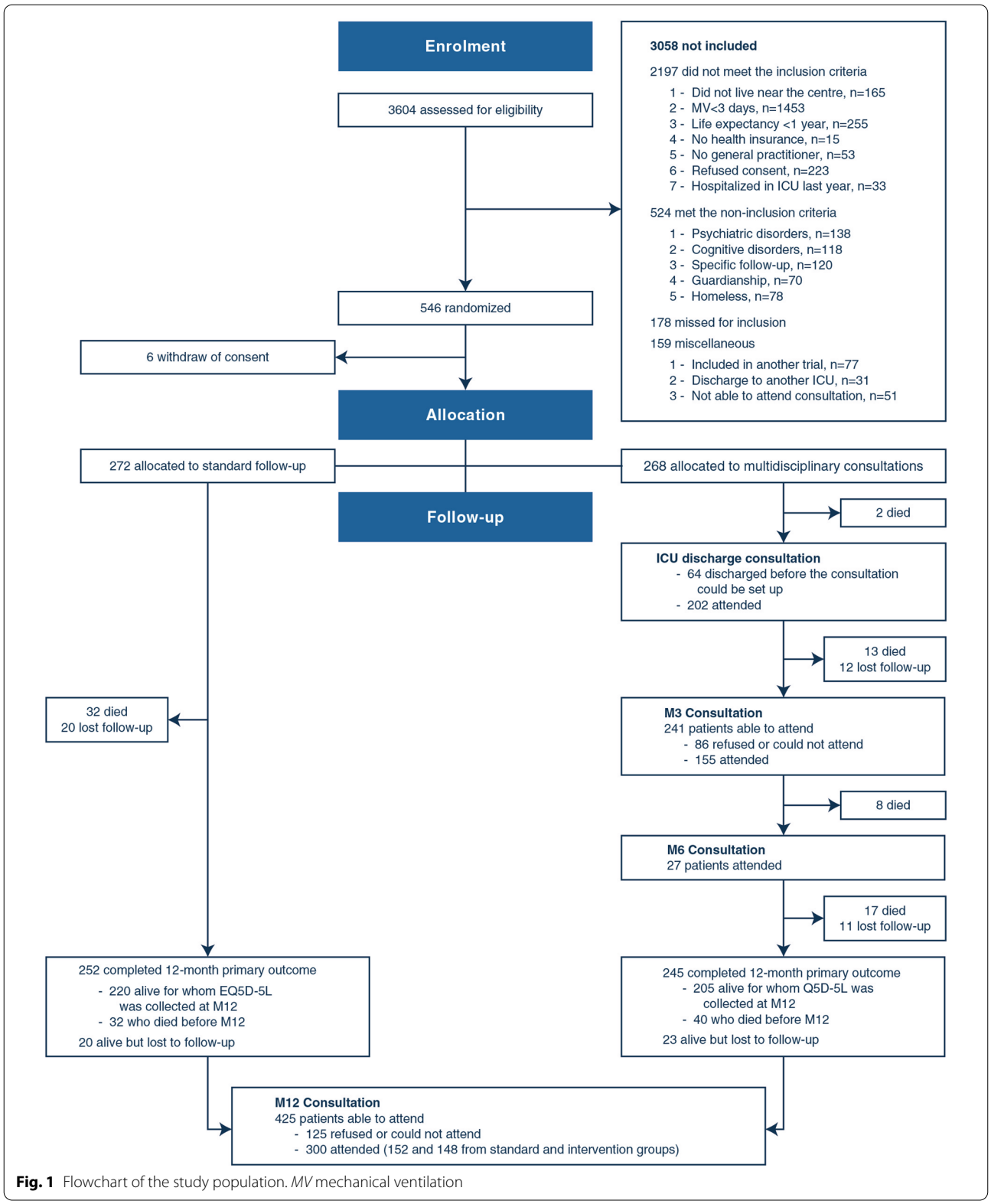

Fig. 1 Flowchart of the study population. *MV* mechanical ventilation

Table 1 Characteristics of study participants at baseline

No. (%) and median (IQR)	*n*	Standard (*n* = 272)	*n*	Multidisciplinary (*n* = 268)
Age at ICU entrance, median (IQR) years	272	64.7 [55.3–75.2]	268	62.4 [51.3–71.7]
Women	272	108 (39.7)	268	103 (38.4)
Charlson comorbidity index	271	3 [2–5]	266	3 [2–5]
Professional status				
Professional activity	243	79 (32.5)	240	78 (32.5)
Unemployed	243	26 (10.7)	240	43 (17.9)
Retired	243	138 (56.8)	240	119 (49.6)
Social status				
Single	217	44 (20.3)	229	41 (17.9)
Married or living as a couple	217	121 (55.8)	229	129 (56.3)
Divorced or Widowed	217	52 (23.9)	229	59 (25.8)
Place of residence				
Home	219	213 (97.3)	230	214 (93)
Nursing home	219	6 (2.7)	230	16 (7)
Admission to ICU				
Type of ICU admission				
Medical	271	233 (86)	267	231 (86.5)
Main cause of critical illness				
Sepsis	270	58 (21.5)	266	50 (18.8)
ARDS	270	25 (9.3)	266	24 (9)
Coma	270	71 (26.3)	267	61 (22.8)
Acute respiratory failure	270	25 (9.3)	267	29 (10.9)
Shock	270	13 (4.8)	267	23 (8.6)
Cardiac disorders	270	14 (5.2)	267	11 (4.1)
Renal failure or metabolic disorders	270	19 (7)	267	10 (3.7)
Liver or digestive disorders	270	15 (5.6)	267	18 (6.7)
Polytraumatism	270	8 (2.9)	267	9 (3.4)
Acute paralysis (including GBS)	270	21 (7.8)	267	27 (10.1)
Others	271	2 (0.07)	268	6 (0.02)
Severity of critical illness				
SAPS II score	272	45 [35–61.0]	266	43 [30–61.8]
SOFA score	266	7 [4–11]	265	7 [4–10]
From ICU admission to discharge				
Time from admission to randomization (days)	271	16 [10–27]	267	15 [10–27]
Duration of mechanical ventilation (days)	272	10 [5–18]	267	9 [6–19]
Length of ICU stay (days)	270	15 [10–26]	267	14 [9–26]
Data at randomization				
Functional status				
MRC-sum score	224	58 [48–60]	226	56 [48–60]
MRC-sum score < 48	224	44 (19.6)	226	51 (22.6)
Barthel index	192	80 [45–95]	200	80 [35–100]
Barthel index ≤ 50/100	192	68 (35.4)	200	71 (35.5)
IADL score	227	4 [1–8]	218	3.5 [1–8]
IADL score ≤ 4	227	120 (52.9)	218	124 (56.9)
Psychological status				
HADS	183	13 [8–19]	206	13.5 [9–20]
HADS anxiety	201	7 [4–10]	213	8 [5–11]
HADS anxiety > 11/21	201	37 (18.4)	213	42 (19.7)
HADS depression	189	6 [3–9]	213	6 [3–10]

Table 1 (continued)

No. (%) and median (IQR)	*n*	Standard (*n* = 272)	*n*	Multidisciplinary (*n* = 268)
HADS depression > 11/21	189	29 (15.3)	213	36 (16.9)
IESR	141	17 [6–38]	167	18 [5.5–38]
IES-R > 37/88	141	38 (27)	167	45 (26.9)
Cognitive status				
MMSE	239	26 [23–29]	237	26 [22–29]
MMSE ≤ 24/30	239	91 (38.1)	237	89 (37.6)
Poor quality of life at 3 months before ICU †	220	66 (30)	221	75 (33.9)
EQ-VAS score 3 months before ICU	218	70 [50–80]	217	70 [50–90]
EQ5D-5L index score 3 months before ICU	218	0.8 [0.5–0.9]	219	0.8 [0.5–1]
Poor quality of life at inclusion†	194	145 (74.7)	200	145 (72.5)
EQ-VAS score at inclusion	201	50 [30–70]	202	50 [30–60]
EQ5D-5L index score at inclusion	181	0.1 [− 0.2 to 0.5]	181	0.1 [− 0.2 to 0.4]
Destination after ICU				
Short stay hospital	259	194 (74.9)	258	195 (75.6)
Mid stay hospital	259	37 (14.3)	258	40 (15.5)
Long stay hospital	259	17 (6.6)	258	15 (5.8)
Rehabilitation center	259	4 (1.5)	258	3 (1.2)
Home	259	7 (2.7)	258	5 (1.9)

ARDS acute respiratory distress syndrome; *BMI* body mass index; *EQ5D-5L* Euro Quality of Life-5 dimensions; *EQ-VAS* Euro Quality of Life-Visual Analogic Scale; *GBS* Guillain-Barré Syndrome, *HADS* hospital anxiety depression scale, *IADL* instrumental activity of daily living, *IES-R* impact of event scale-revised, *IQR* interquartile range, *MMS* minimal mental state, MRC-sum score medical research council-sum score, *SAPSII* simplified acute physiological score II; *SOFA* sequential organ failure assessment, *VAS* visual analogue scale

† Poor quality of life was defined as a severe-to-extreme impairment on at least one of the EQ5D-5L dimensions

EQ5D-5L index score at M12 was significantly lower in the multidisciplinary than in the standard group (0.5 [0–0.8] *versus* 0.6 [0.3–0.9], $p = 0.03$) (Table 3).

Among the 425 patients who were convened to the M12 consultation, 300 (70.6%) attended (152 and 148 patients in the standard and multidisciplinary group, respectively). Functional, psychological, and cognitive status did not statistically differ between groups at M12 (Table 3 and Tables S11, ESM). Among the patients, who, at the M12 consultation were previously advised to seek for medical, social, or psychological support, 85% of them followed the advice. Although more than 90% of patients rated the quality of care they received during the year as good or excellent, about half of them reported that their needs had not been met in both groups (Table S12, ESM).

Discussion

This study showed that, in comparison with a community follow-up, a hospital-based face-to-face multidisciplinary post-ICU consultation has unexpectedly a detrimental effect on the QoL but was not associated with a lower improvement in the functional, psychological, and cognitive status, at 1 year.

This finding does not follow the same trend as most previous trials. Until now, studies either reported no effect on the QoL [23, 25, 27, 34–36, 36–40], a physical benefit [37], or a reduction in mortality [41] Also, the two main meta-analyses provided conflicting results [26, 28]. Comparison between RCT is difficult due to methodological discrepancies, particularly in terms of intervention practical programs (including organization, staff training, and the type of care provided) [26, 28]. In most trials testing a multidisciplinary approach, post-ICU follow-up was organized by specifically trained nurses, who saw patients face-to-face and reported to other consultants from different specialties [23, 25, 34, 40]. In our study, nurses were not involved, and the patients were systematically seen by an ICU physician, a psychologist, and a social worker. In previous trials, the intervention program targeted the psychological [23, 34, 40], cognitive [23], or physical domains [23, 24, 27, 35], nutritional rehabilitation [27], or the family environment [25], either separately or combined.

The multidisciplinary consultation was associated with a degradation on the anxiety/depression dimension, suggesting that the intervention had a negative psychological effect, even if the HADS and IES-R at 12 months did not reflect it. The patient's expectations may have been disappointed, as the multidisciplinary intervention did not objectively translate into improved clinical recovery and well-being. Also, the bias might have been amplified

Table 2 Characteristics at 3 months of patients included in multidisciplinary group

Characteristics	Population	No (%) or median (IQR)
Patients not able to attend the consultation	268	27 (10.1)
Death	27	15 (55.6)
Lost to follow-up	27	12 (44.4)
Patients able to attend the consultation	268	241 (89.9)
Patients who attended	241	155 (64.3)
Patients who did not attended	241	86 (35.7)
Time from randomization to M3 consultation-days	155	103 [92–145.2]
Functional status at 3 months	155	
MRC-sum score	128 (82.6)	60 [54–60]
MRC-sum score < 48	128 (82.6)	17 (13.3)
Barthel index	128 (82.6)	100 [90–100]
IADL score	130 (83.9)	8 [4–9]
Psychological status at 3 months	155	
HADS	131 (84.5)	11 [6–16]
IES-R	127 (81.9)	11 [3–23.5]
Cognitive status at 3 months	155	
MMS	133 (85.8)	29 [26–30]
Clinical assessment	155	
BMI	96 (61.9)	25.3 [21.8–31.1]
General symptoms	135 (87.1)	82 (60.7)
Asthenia		54 (40)
Weight loss		24 (17.8)
Change in general condition		13 (9.6)
Chest/respiratory symptoms	138 (89)	76 (55.1)
Dyspnea		47 (34.1)
Cough		25 (18.1)
Pain		6 (4.3)
Cardiologic symptoms	138 (89)	45 (32.6)
Pain		7 (5.1)
Hypertension		24 (17.4)
Heart failure		9 (6.5)
Digestive symptoms	137 (88.4)	41 (29.9)
Pain		13 (9.5)
Transit disorders		17 (12.4)
Appetite loss		9 (6.6)
Neurological symptoms	135 (87.1)	68 (50.4)
Headache		7 (5.2)
Motor deficit		37 (27.4)
Sensory disorders		31 (23)
Confusion		1 (0.7)
Decision of multidisciplinary staff	155 (100)	
Paraclinical explorations		6 (3.9)
Change to therapy		11 (7.1)
Hospitalization		8 (5.2)
Referred to a physician		41 (26.5)
Referred to psychologist/psychiatrist		34 (21.9)
Referred to a social worker		36 (23.2)
To be seen again at 6 months		28 (18.1)
Patients followed up at 6 months		27 (17.4)

BMI body mass index, *HADS* hospital anxiety depression scale, *IADL* instrumental activity of daily living, *IES-R* impact of event scale-revised, *IQR* interquartile range, *MMS* minimal mental state, *MRC-sum score* medical research council-sum score, *VAS* visual analogue scale

Table 3 Primary and secondary outcomes

No. (%) or median (IQR)	*n*	Standard	*n*	Multi disciplinary	Unadjusted OR[*] (95% CI)	Adjusted OR[*Θ] (95% CI)	*p* value
Primary outcome[†α]							
Intention to treat	272		268		1.44 [1.02–2.04]	1.49 [1.04–2.13]	0.04[a] 0.03[b]
No. (%) or median (IQR)		***n***		**Standard**	***n***	**Multi disciplinary**	***p* value**
Secondary outcomes							
Quality of life							
Death during follow-up[α]		272		32 (11.8)	268	40 (14.9)	0.34
Poor QoL[£]		220		72 (32.7)	205	82 (40)	0.14
EQ-VAS score		220		70 [50–80]	207	70 [50–80]	0.36
EQ5D-5L index score		251		0.6 [0.3–0.9]	243	0.5 [0–0.8]	0.03
M12 consultation[§]							
Attendees		152			148		
Days from inclusion		150		384.5 [365–426.8]	136	391.5 [369.5–435]	
Functional status[§]							
MRC-sum score		120		60 [58–60]	108	60 [57.5–60]	0.92
Barthel index		127		100 [95–100]	113	100 [95–100]	0.99
IADL score		122		8 [7–9]	114	8 [6–9]	0.57
Psychological status[§]							
HADS		130		9 [6–15]	127	10 [5–16.5]	0.32
HADS anxiety		134		5 [3–8]	128	6 [3–9]	0.68
HADS depression		133		4 [1–7]	128	4 [2–8]	0.15
IES-R		121		8 [2–20]	120	7.5 [1.8–20.2]	0.99
Cognitive status [§]							
MMS		128		29 [27–30]	115	29 [27–30]	0.83
Social status[§∞]							
Return to home		202		178 (88.1)	198	163 (82.3)	0.14
Return to work[π]		79		32 (40.5)	78	24 (30.8)	0.27
Care provided within 12 months[§∞]							
At least one outpatient consultation		134		101 (75.4)	219	138[μ] (63)	0.02
At least one hospitalization		135		48 (35.6)	223	88[μ] (39.5)	0.53
Number of hospitalizations				1 [1–2]	134	1 [1–1]	0.36

CI confidence interval, *EQ5D* Euro Quality of Life–5 dimensions, *HADS* hospital anxiety depression scale, *IADL* instrumental activity of daily living, *IES-R* impact of event scale-revised, *IQR* interquartile range, *MMS* minimal mental state, *MRC-sum score* medical research council-sum score, *OR* odds ratio, *SOFA* sequential organ failure assessment, *VAS* visual analogue scale

[†] Primary outcome was defined by death or severe-to-extreme impairment on at least one dimension of the EQ5D-5L. It was collected by phone

[α] The time in months from randomization to the phone collection of the primary endpoint (i.e., EQ5D at 1 year) was 12.3 [11.9–13.4] in the whole population

[*] Multiple imputation was performed for the intention to treat analysis. The proportion of patients with a bad outcome ranged between 42.3% and 44.1% in the standard group and between 52.6% and 53.7% in the multidisciplinary group, among the imputed datasets

[Θ] Analysis adjusted for age and SOFA at admission

[£] Only in patients who had not died. Poor quality of life was defined as a severe-to-extreme impairment on at least one dimension of the EQ5D-5L

[a] p value in the unadjusted model. [b] p value in the adjusted model

[¥] Categorical variables were compared with using the Chi-square or Fisher's exact test and quantitative variables with using the Student's *t* or Wilcoxon tests, as appropriate

[§] Functional, psychological, cognitive, social status, and care provided within the 12 months were collected in patients who attended the M12 consultations

[π] Among the 157 patients who were professionally active before their ICU admission

[μ] 226 patients in the intervention groups benefited from an outpatient clinic or hospitalization, which were initiated by the multidisciplinary team in 96 patients (42%)

[∞] This information was collected at M3, M6, and M12 in the multidisciplinary group and only at M12 in the standard group

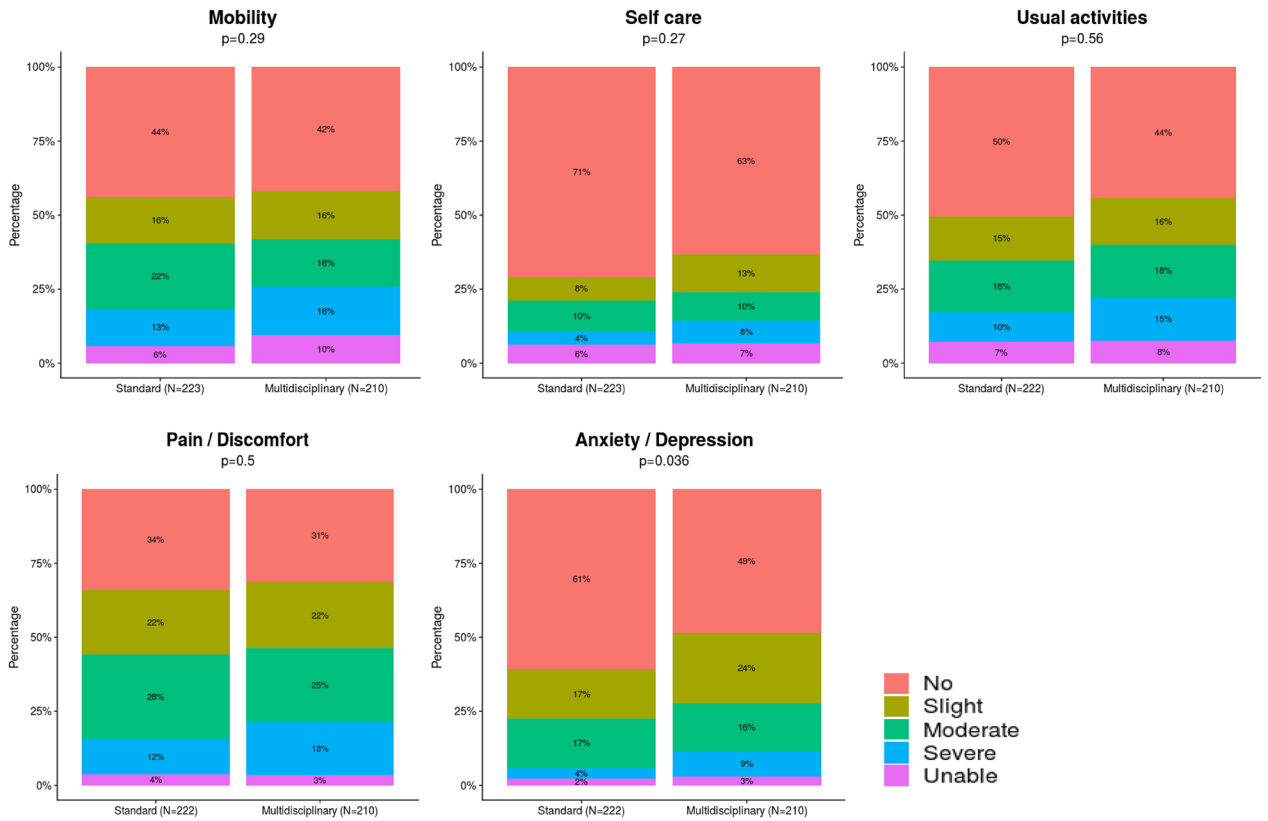

Fig. 2 Comparison of the distribution of EQ5D-5L at 12 months between standard and multidisciplinary groups

by the inherent characteristic of the EQ5D-5L to be a patient reported scale.

Furthermore, potential benefits of multidisciplinary consultations could have been offset by the refusal rate of 36% to come to the M3 multidisciplinary consultation. However, this absentee rate remains within the range reported in previous trials, varying from 25% [26] to 37% [27]. Interestingly, the patients who did not attend the M3 consultations had a better QoL and functional status at randomization but were more anxious and depressed. This profile may have made them more reluctant to attend multidisciplinary consultations. Finally, small differences in baseline characteristics between the two groups were observed which that could result in a difference in QoL at 1 year.

Our trial has various limits. First, our trial was designed based on expert opinions, due to the lack of observational data on post-ICU needs and trajectories in France. Second, we did not directly confirm with the GP, the community psychologist or social worker, whether they had followed the recommendations of the multidisciplinary team. However, almost all patients reported that they have respected them. A closer interaction with the community caregivers or the patient himself might have resulted in better outcomes for patients. The involvement of the multidisciplinary team was not only observational and could result in specific recommendations. Those might not address the patient's complains which mainly appeared to be linked to general symptoms, for which no specific measures could be considered.

Consequently, multidisciplinary consultations might not have been appropriately designed for improving QoL. Also, because medical consultations were performed by intensivists, who are usually not trained for handling general symptoms such as asthenia or cognitive impairment, those have not been adequately assessed and managed. However, it was not feasible to add a comprehensive cognitive assessment, as it would have been too time-consuming for the patients, given that the medical and psycho-social consultation already lasted about 2 h. It is unlikely that cognitive impairment was less frequent or severe in the patients who received standard follow-up, since baseline characteristics were comparable between the two groups. Similarly, physiotherapists were not systematically involved, while previous trials showed that a rehabilitation program could improve functional outcomes [36, 37]. Nonetheless, functional status did not differ between the two groups. Our results are probably

generalizable to most health care systems of post-industrial countries. As we found that standard care had a better impact on QoL, the outcomes might be opposite in an environment where community care is not optimal.

Finally, our definition of poor QoL is not commonly used. Nevertheless, our post hoc analysis showed that the multidisciplinary consultation was significantly associated with lower EQ5D-5L index score, confirming its negative impact. Moreover, a 0.1 point difference in EQ5D-5L index score between the two groups is considered clinically relevant [44]. It is noteworthy that the detrimental effect of the multidisciplinary intervention remains when a moderate degradation of the QoL is included in the definition of the primary outcome or when the EQ5D-5L "3 months before ICU" is considered as an adjustment variable.

In conclusion, our RCT shows that our program of hospital-based, face-to-face, intensivist-led multidisciplinary consultations was associated with poor outcome at 1 year after ICU discharge, impacting notably the anxiety/depression domain of QoL. Other post-ICU strategies for addressing the unsatisfied needs of ICU survivors await further evaluation.

Supplementary Information

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Author contributions
DF and TS: conception of the work (PI), funding application, enrollment of participating centers, supervision of the data collection, participation in data analysis verification of the data and interpretation, writing of the manuscript, and critical revision of the manuscript. LG: methodology and data management. LN and LG: statistical analysis. AM: interpretation of the results, writing of the manuscript, and critical revision of the manuscript. Other authors: patients' recruitment and data collection.

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Availability of data and materials
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Declarations

Conflicts of interest
RS received grants from the French Ministry of Health, the French Society of Intensive Care Medicine (SRLF), and the European Society of Intensive Care Medicine (ESICM). All other authors declare no conflicts of interest.

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