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Sounding the Alarm: What Clinicians Need to Know about Physical, Emotional, and Cognitive Recovery After Venoarterial Extracorporeal Membrane Oxygenation

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Abstract

OBJECTIVE: We summarize the existing data on the occurrence of physical, emotional, and cognitive dysfunction associated with postintensive care syndrome (PICS) in adult survivors of venoarterial extracorporeal membrane oxygenation (VA-ECMO).

DATA SOURCES: MEDLINE, Cochrane Library, EMBASE, Web of Science, and CINAHL databases were searched.

STUDY SELECTION: Peer-reviewed studies of adults receiving VA-ECMO for any reason with at least one measure of health-related quality of life outcomes or PICS at long-term follow-up of at least 6 months were included.

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DATA EXTRACTION: The participant demographics and baseline characteristics, in-hospital outcomes, long-term health outcomes, quality of life outcome measures, and prevalence of PICS were extracted.

DATA SYNTHESIS: Twenty-seven studies met inclusion criteria encompassing 3,271 patients who were treated with VA-ECMO. The studies were limited to single- or two-center studies. Outcomes variables and follow-up time points evaluated were widely heterogeneous which limits comprehensive analysis of PICS after VA-ECMO. In general, the longer-term PICS-related outcomes of survivors of VA-ECMO were worse than the general population, and approaching that of patients with chronic disease. Available studies identified high rates of abnormal 6-minute walk distance, depression, anxiety, and posttraumatic stress disorder that persisted for years. Half or fewer survivors return to work years after discharge. Only 2 of 27 studies examined cognitive outcomes and no studies evaluated cognitive dysfunction within the first year of recovery. No studies evaluated the impact of targeted interventions on these outcomes.

CONCLUSIONS: Survivors of VA-ECMO represent a population of critically ill patients at high risk for deficits in physical, emotional, and cognitive function related to PICS. This systematic review highlights the alarming reality that PICS and in particular, neurocognitive outcomes, in survivors of VA-ECMO are understudied, underrecognized, and thus likely undertreated. These results underscore the imperative that we look beyond survival to focus on understanding the burden of survivorship with the goal of optimizing recovery and outcomes after these life-saving interventions. Future prospective, multicenter, longitudinal studies in recovery after VA-ECMO are justified.

Keywords

health-related quality of life; long-term venoarterial extracorporeal membrane oxygenation; outcomes; postintensive care syndrome

Postintensive care syndrome (PICS) is characterized by new or worsening symptoms or impairments in physical, emotional, and/or cognitive health in survivors of critical illness (1). After discharge from a medical or surgical ICU, 56–96% of survivors report impairment in at least one PICS domain that can persist past 6–12 months (2, 3). Among patients surviving discharge from the cardiac intensive care unit, 92% had problems in at least one PICS domain at 12 weeks following hospital discharge (4). The sequelae of PICS include increased posthospitalization mortality, high rates of post-ICU healthcare utilization, lost employment, decreased quality of life, significant healthcare expenses, and a concomitant and substantial impact on caregivers (5).

Patients treated with both venovenous (VV) and venoarterial (VA) extracorporeal membrane oxygenation (ECMO) are at high risk for PICS. During the COVID-19 pandemic, Outcomes and Recovery After Critical Illness Leading to ECMO (ORACLE), a multidisciplinary collaboration across academic medical centers, looked at posthospitalization recovery in survivors of respiratory failure from COVID-19 treated with VV-ECMO versus mechanical ventilation alone (6, 7). Of survivors with documented follow-up at 4 months, 95% were living at home, but only one in four survivors were back to work or usual activity. Depression, anxiety, or posttraumatic stress disorder (PTSD) were less frequently screened

for but present in one-third of those tested. ICU-acquired weakness was present in one-half of the survivors and nearly all of the survivors who were assessed had an abnormal 6-minute walk distance. One-quarter of patients still required supplemental oxygen and nearly half of those tested had abnormal spirometry. With regard to cognitive dysfunction specifically, an alarming 88% of the ECMO cohort screened, compared with 60% of those screened in the ventilated-only group, p equals 0.26, had cognitive dysfunction. Although likely underpowered to definitively assess differences between these cohorts, it remains concerning that cognitive impairment was identified in the majority of survivors of VV-ECMO (7).

Compared with patients treated with VV-ECMO, patients requiring venoarterial extracorporeal membrane oxygenation (VA-ECMO) are in cardiogenic shock requiring mechanical support for survival. These patients experience significant morbidity and mortality upwards of 50%. Posthospitalization survival requires either recovery, heart transplant (HTx), or bridge to durable mechanical support. Existing literature about patients treated with venoarterial extracorporeal membrane oxygenation (VA-ECMO) focuses on predictors related to in-hospital morbidity and mortality (8–11). Fewer studies examine health-related quality of life (HRQOL) outcomes, and to our knowledge, no studies have characterized PICS in survivors of VA-ECMO. Herein, the ORACLE group performed a systematic review of the literature to summarize the existing data on the occurrence of PICS-related deficits in adult survivors of VA-ECMO.

MATERIALS AND METHODS

A systematic review (International Prospective Register of Systematic Reviews registration CRD42021290471) was conducted (Fig. 1) following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. MEDLINE, Cochrane Library, EMBASE, Web of Science, and CINAHL databases were searched for peer-reviewed studies of adults receiving VA-ECMO with at least one measure of HRQOL outcomes or PICS at long-term follow-up of at least 6 months. Inclusion and exclusion criteria and processes for evaluating studies are presented in Supplemental Methods (<http://links.lww.com/CCM/H340>). Risk of bias analysis was performed using the Newcastle-Ottawa Scale (12).

Primary outcomes were HRQOL outcomes and occurrence of impairments related to PICS in physical, mental health, and cognitive domains. The instruments used are summarized in Supplemental Methods (<http://links.lww.com/CCM/H340>). Secondary outcomes included in-hospital outcomes, long-term health outcomes, and healthcare costs. In-hospital and ICU lengths of stay, duration of ECMO run, duration of ventilation, occurrence of complications, and mortality were extracted.

Statistical Considerations

Descriptive statistics including frequencies and percentages, central tendencies, and variances of sample characteristics and outcomes were recorded from each population and pooled based on mean and SD. For studies reporting median values and interquartile range, the mean and SD were estimated, weighted by sample size (13, 14). Pooled mean and SD calculations were weighted for study sample size using Arsham's formula (15).

Meta-analyses were not feasible due to the limited quantitative data and heterogeneity in reporting of outcomes across study populations, and because there was not always a control group or effect size reported by each study.

RESULTS

Summary of Studies

A total of 429 peer-reviewed studies were screened, and 27 met inclusion criteria (Fig. 1; Supplemental Table 1, <http://links.lww.com/CCM/H340>). Studies were single- or two-center and retrospective. Twenty-five performed cohort analyses, 2 provided descriptive reports, 23 were cross-sectional, and 4 were longitudinal (Supplemental Table 1, <http://links.lww.com/CCM/H340>). All studies were of good or fair quality in risk of bias analysis and therefore were included in this review (Supplemental Table 2, <http://links.lww.com/CCM/H340>). The indications for VA-ECMO, in-hospital outcomes measured, instruments used to measure physical, mental, and cognitive HRQOL outcomes, reporting of return to work and cost, as well as follow-up period were heterogeneous, and not a single study looked at all variables (Fig. 2).

In-Hospital Outcomes

In-hospital outcomes were reported by 25 of the 27 studies for a total of 3,243 patients who were on VA-ECMO (Supplemental Table 3, <http://links.lww.com/CCM/H340>). The pooled mean age was 57 years and 64.4% were male. Pooled analysis revealed a mean of 5.8 days on VA-ECMO, 13.1 days of mechanical ventilation, 17.9 days in the ICU, and 37.3 days in the hospital. The overall hospital survival rate was 39.7%. Of all patients treated with VA-ECMO, 7.5% were bridged to VAD, 6.1% were bridged to HTx, and 44.3% suffered ECMO-related complications.

Physical Outcomes

Several studies addressed physical outcomes through transthoracic echocardiography measurements of left ventricular ejection fraction (LVEF), the 6-minute walk test (6MWT), an objective measure of functional exercise capacity (16), and self-reported measures of functional status, including the New York Heart Association (NYHA) Functional Status (17), the Barthel Index for activities of daily living (ADL) (18), and the modified Rankin Scale (mRS) (19) (Table 1).

Cardiac Function.—Six studies (20–26) assessed LVEF. Five studies reported pre-ECMO LVEF for a total of 281 patients with a pooled mean LVEF of $25.6\% \pm 12.3\%$. Six studies reported the LVEF for a total of 169 VA-ECMO survivors at an average follow-up of 25 ± 12 months with a pooled mean LVEF of $52.3\% \pm 11.1\%$. Four studies reported LVEF pre-ECMO and at long-term follow-up, of which three showed improved LVEF at follow-up (pooled $18.8\% \pm 10.9\%$ to $57.3\% \pm 4.8\%$) and one showed unchanged LVEF at follow-up ($50\% \pm 16\%$ to $56\% \pm 11\%$).

6-Minute Walk Test.—Only one study (24) used the 6MWT for 21 survivors at a median follow-up of 2.6 years (IQR 1.7–4.0 yr). The median 6MW distance was notably 68.8%

(IQR 61.7–91.6%) of predicted, and two patients had to terminate the 6MWT due to dizziness or dyspnea.

Functional Status.—Seven studies (24–30) assessed NYHA Functional Status (17). Only two studies assessed pre-ECMO NYHA Functional Status, where 55% of 154 patients were NYHA class III or IV (marked or severe limitations in activity). All seven studies reported NYHA Functional Status at a mean follow-up of 30 ± 18 months and found that the majority (88%) of the 142 survivors were NYHA class I or II (no or slight limitations in activity). Schoenrath et al (31) reported a mean Barthel Index of 98/100, indicating total independence among 16 survivors at a mean follow-up of 34 months, almost 3 years out from discharge after VA-ECMO. Guenther et al (24) found that 94% of 36 VA-ECMO survivors reported an mRS less than or equal to 2 (free from moderate to severe disability) at median follow-up of 2.6 years. Corsi et al (32) found that none of the seven survivors experienced chronic dyspnea and two of the seven had moderate limitations in instrumental ADLs due to lower limb/toe amputation at median follow-up of 19 months.

Return to Work.—Ten of 27 studies (22, 24, 29, 32–38) assessed the ability of 392 VA-ECMO survivors to return to work, at average follow-up of 40 ± 22 months. Despite the seemingly optimistic reported functional recovery above, four studies (29, 32, 37, 38) found that only 19% of survivors were working or studying at follow-up without considering prior status. Four studies (24, 33–35) found that 39–57% of survivors who were less than 60–65 years old had returned to work or school at follow-up. Two studies (22, 36) found that 41% of VA-ECMO survivors who were previously working had returned to work at follow-up. One study (38) reported that the average time to return to work was 16 ± 9 months after discharge.

Disposition.—Only three studies commented on disposition at discharge with highly variable. One study (24) reported 11% of 79 patients were discharged home, while another (22) reported 71% of 14 patients were discharged home. One study (35) reported 23% of 48 VA-ECMO survivors needed rehabilitation at discharge and another (24) reported 97% of the 79 VA-ECMO survivors received rehabilitation between discharge and median follow-up of 1.9 years. Four studies looked at living situation, mean follow-up of 27 ± 11 months, with 0–22% requiring home health care (34, 35) (24) (36).

Mental Health Outcomes

Seven of 27 studies evaluated mental health outcomes with either the Hospital Anxiety and Depression Scale (39), Depression Patient Health Questionnaire 9 (40), Beck Depression Inventory, second edition (41), and the Impact of Event Scale, Revised (42) (Table 1). In the seven studies reporting psychological outcomes, ECMO duration averaged less than 7 days, with some survivors having ECMO durations approaching 2 weeks. The studies span a range of indications for VA-ECMO including postcardiotomy, primary heart failure, sepsis-related heart failure, acute cardiovascular collapse related to pulmonary embolism, and hypothermia. Across five studies (8, 21, 22, 32, 36), 35% of 109 VA-ECMO survivors had significant to severe symptoms of anxiety at an average follow-up of 29 ± 18 months. Across seven studies (8, 21, 22, 24, 29, 32, 36), 26% of 152 survivors had symptoms of

depression at an average follow-up of 30 ± 19 months. Across seven studies (8, 21, 22, 32, 36, 43, 44), 21% of 158 survivors were at risk for PTSD at an average follow-up of 33 ± 18 months. One study (45) reported that 71.4% of 20 survivors had sleeping disturbances at follow-up of up to 3 years. One study (43) reported that 18% of survivors had preexisting psychiatric histories before being placed on VA-ECMO. One study (22) reported that 5 of 10 VA-ECMO survivors were receiving psychologic support at a median follow-up of 13 months.

Cognitive Outcomes

Only 2 of 27 studies (24, 38) assessed cognitive outcomes among 64 VA-ECMO survivors, at an average follow-up of 67 ± 30 months (Table 1). One study (38) performed neurocognitive testing including the full-scale intelligence quotient, memory index, and executive index. Twenty-eight patients underwent full neurocognitive evaluation at a median follow-up of 9 years (range 3.1–17.1 years) and all patients fell within 2 SDS of normal for global, memory, and executive function. The other study (24) used the Montreal Cognitive Assessment (46) for 36 survivors at a median follow-up of 2.6 years. The median score was 26.0 (IQR 22.5–28.0), the lower limit of normal; however, the study did not state how many individuals scored outside of the normal range.

General Health-Related Quality of Life

Most studies (22 of the 27) used general HRQOL questionnaires that address patient perception of both physical and mental health outcomes: the Short Form 36-Item Health Survey (SF-36), the EuroQOL 5-dimension questionnaire (EQ-5D), and World Health Organization QOL (WHOQOL). The SF-36 evaluates eight domains including physical functioning (PF), role limitations due to physical health problems (RP), role limitation due to emotional problems (RE), social functioning (SF), bodily pain (BP), energy/fatigue or vitality (VT), emotional well-being or mental health (MH), and general health perceptions (GH), and assigns summary scores, physical component summary (PCS), and mental component summary.

Short Form 36-Item Health Survey.—Fifteen studies (8, 21–24, 26, 29, 31, 32, 34, 36, 37, 44, 47, 48) used the SF-36, of which 13 compared SF-36 results with a general population. Compared with the general population, VA-ECMO survivors experienced worse physical and mental health QOL outcomes across the different domains (Fig. 3A). In contrast, nine studies (21–24, 29, 32, 34, 47, 48) compared SF-36 results with critically ill patients or patients with chronic disease and found VA-ECMO survivors had comparable or better physical and mental health QOL outcomes (Fig. 3B). Two studies compared patients with postcardiotomy cardiogenic shock who required or did not require VA-ECMO (26, 37) and found patients who required VA-ECMO had significantly worse HRQOL outcomes in domains encompassing both physical and mental health.

Three studies (8, 23, 37) compared SF-36 domains among VA-ECMO survivors stratified based on follow-up period. Combes et al compared cohorts at less than 325 days vs. 325 days (0.9 yr) and saw significantly higher scores in seven of the eight SF-36 domains (all except the MH domain) and the PCS summary score in the latter cohort. Muller et al

compared cohorts at less than 945 days versus those greater than or equal to 945 days (2.6 yr) and saw significantly higher scores in three domains (PF, RP, and SF) in the latter cohort. Shao et al compared SF-36 scores in the first, third, and fifth year of follow-up, and found significantly higher scores in three domains (BP, VT, and MH) in the third versus first year of follow-up but did not see any difference between the third versus fifth year of follow-up.

EuroQOL 5-Dimension Questionnaire.—Seven studies (20, 27, 33–35, 43, 49) used the EQ-5D for 266 VA-ECMO survivors, with an average follow-up of 33.8 ± 23.2 months. Three studies compared the EQ mean index score of VA-ECMO survivors to the general population: 2 [34, 35] found no significant difference and 1 [33] found worse scores among survivors. Across four studies (33–35, 49), the pooled EQ mean index score for survivors was 0.75 ± 0.18 . Across four studies (27, 34, 43, 49) the pooled EQ visual analog scale (VAS) score for survivors was 71.8 ± 11.4 . Both the EQ mean index score and EQ VAS are comparable to similarly aged people in the general population (50). Two studies (33, 49) reported results for individual EQ dimensions. Among 89 survivors at an average follow-up of 49.2 ± 43.4 months, 51% experienced some to severe problems in life-mobility, 24% in self-care, 43% in usual activities, 63% in pain and discomfort, and 40% in anxiety and depression. Compared with the general population (50), VA-ECMO survivors have a higher prevalence of problems in the life-mobility, self-care, and usual activities dimensions.

Berger et al (20) looked at patients who received ventricular assist device (VAD) with or without VA-ECMO before VAD and performed longitudinal analysis with EQ-5D at 3, 6, and 12 months after VAD implantation and last follow-up at the time of the study. Although there was a trend in improvement of the EQ-5D score over time, these were not statistically significant.

WHOQOL.—Tseng et al performed longitudinal analysis on overall HRQOL using WHOQOL with additional questions for working competence and physical function for ADL in HTx recipients with or without preoperative ECMO (45, 51). In general, they found that overall HRQOL, working competence, or physical function for ADL improved over time and that HTx recipients with preoperative ECMO had worse scores.

Costs

A single study (35) looked at healthcare costs. The study was done in Finland for all causes of VA-ECMO across 102 patients, with median hospital LOS of 32 days and about 30% of patients requiring rehabilitation at discharge. The median in-hospital cost per patient was \$142,000 and the median hospital-related costs per person within the first year following the index hospitalization was \$18,000. The predicted mean quality-adjusted life years (QALYs) gained with VA-ECMO was 21, with a median cost per QALY of \$8,200.

DISCUSSION

Though there are no studies that comprehensively and longitudinally assess physical, emotional, and cognitive deficits associated with PICS in survivors after VA-ECMO, this systematic review reveals that deficits in PICS-related domains are measurable in survivors of VA-ECMO and can impact quality of life and return to function for years after discharge

(Fig. 4). The pooled characteristics of the cohort (mean 5.8 d on VA-ECMO, 13.1 d of mechanical ventilation, 17.9 d in the ICU, and 37.3 d in the hospital) are similar before meta-analyses (9), suggesting that the studies reviewed are appropriately representative. All studies had a follow-up of at least 6 months. This systematic review highlights the heterogeneity of instruments used to evaluate physical and mental health outcomes and the need to employ consensus screening tools and time points in the postintensive care period. In addition, this review also underscores the limitations of small- to medium-sized studies from one or two participating centers. Compared with the international Extracorporeal Life Support Organization registry where participating ECMO centers cooperate and report survival data, this review exposes the lack of infrastructure to track the physical, emotional, and cognitive recovery of survivors of this resource-intensive, increasingly used, life-saving intervention.

Regarding physical outcomes, despite near-normal heart function, VA-ECMO survivors achieved only 69% of the predicted 6-minute walk distance at a median follow-up of 2.6 years, similar to survivors of critical illness who achieve 60–81% of predicted 6-minute walk distance at 1–5 years follow-up (52) and patients following cardiac surgery 74% of predicted 6-minute walk distance at median 23 months follow-up (53). A 6-minute walk distance of less than 96% is predicted to identify individuals with low cardiorespiratory fitness (54). Despite most survivors reporting NYHA class I-II symptoms at follow-up, less than half had returned to work more than 1 year after discharge. The reported receipt of rehabilitation was variable (23–97%), with limited information about timing, frequency, modality, and duration. Importantly, no studies investigated if rehabilitation interventions are associated with, predict, or improve quality of life or PICS-related outcomes among VA-ECMO survivors.

VA-ECMO survivors experience a high burden of mental health impairments. Thirty-five percent reported significant to severe symptoms of anxiety at mean follow-up of 29 months, similar to 34% of adult ICU survivors at 12- to 14-months postdischarge (55) and 38% of survivors of acute respiratory distress syndrome (ARDS) at greater than 12-month follow-up (56), slightly higher than the 24% of patients with prolonged ICU length of stay at 3–6 months after cardiac surgery (57), and nearly 10 times higher than the 3.6% global prevalence of anxiety (58). Twenty-six percent of VA-ECMO survivors reported symptoms of depression, similar to 29% of adult ICU survivors at 12–14 months postdischarge (59) and 32% of survivors of ARDS at greater than 12-month follow-up (56), and higher than the 17% of patients with prolonged ICU length of stay at 3–6 months after cardiac surgery (57), and nearly six times higher than the 4.4% global prevalence of depression (58). Twenty-one percent of VA-ECMO survivors were at risk for PTSD, similar to 20% of adult survivors of critical illness at greater than 12 months postdischarge (60), 23% of survivors of ARDS at greater than 12-month follow-up (56), and 18.2% at 6 months after cardiac surgery (61), but more than five times higher than the 3.9% global lifetime prevalence of PTSD (62). There are little data on changes in mental health over time and the impact of psychological support interventions on mental health.

Cognitive outcomes among VA-ECMO survivors were shockingly limited. Cognitive test results were reported in only two studies with small sample sizes that were within the

normal range for at least some proportion of patients several years after discharge. No studies looked at cognitive outcomes within the first year after discharge. Among survivors of critical illness, up to 40% have cognitive impairment at 3 months follow-up (63) and following coronary artery bypass surgery, 24% and 42% of patient experience cognitive decline from their baseline testing at 6 months and 5 years, respectively (64). In survivors of COVID-19 treated with VV-ECMO, 88% of those screened had cognitive impairment in the first 4 months after discharge. Given the limited data concerning cognitive outcomes following VA-ECMO, it is hard to draw any conclusions. Clearly this topic warrants further investigation.

VA-ECMO survivors experience a range of HRQOL, from normal to severe depending on the domain. Physical, mental, and cognitive impairments can persist for years after discharge. There are limited longitudinal data and virtually no data on how targeted interventions may improve long-term outcomes in these patients. Future prospective longitudinal studies in recovery after VA-ECMO are justified.

LIMITATIONS

An expected limitation is that no patients had PICS screening to assess their baseline before emergent VA-ECMO. The instruments used to measure HRQOL outcomes and the time points for follow-up were very heterogeneous. In most cases, actual values were unavailable, thus prohibiting a meta-analysis. Most measures were retrospective and self-reported, which could result in recall bias. One or two-center studies and small sample sizes limit the generalizability of the results. The use of age- and sex-matched controls varied between cohort studies, thus limiting their interpretation. Finally, there is little to no granularity in reported outcomes between LVAD, transplant, and recovered survivors.

FUTURE DIRECTIONS

Patients treated with VA-ECMO represent a population of critically ill patients at high risk for PICS-related deficits. This systematic review underscores the limited comprehensive data on longitudinal outcomes in VA-ECMO survivors. Understanding longitudinal outcomes in addition to associated targeted interventions is crucial to advancing our understanding of recovery in these critically ill patients. This review certainly highlights the need for a more comprehensive, prospective, multicenter study. Applying consensus screening tools to assess survivors of VA-ECMO can help overcome this severe knowledge gap related to this unique population of survivors (65). These data can inform patient selection and our subsequent in-hospital and posthospitalization management. Mere survival is no longer the end game. Optimizing physical, emotional, and cognitive recovery is the expanding horizon for patient and family expectations. It is imperative that clinicians rise to this challenge and not only command the data on our long-term outcomes but push the forefront of innovative research to optimize this recovery.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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KEY POINTS**Question:**

This study summarizes existing data on the physical, emotional, and cognitive dysfunction associated with postintensive care syndrome (PICS) in adult survivors of venoarterial extracorporeal membrane oxygenation (VA-ECMO).

Findings:

This systematic review revealed the limited data on the occurrence and trajectory of PICS among survivors of VA-ECMO. Survivors of VA-ECMO are at high risk for developing the long-term deficits associated with PICS with consequences that are poorly understood.

Meaning:

Prospective studies are required to understand the PICS-related deficits in survivors of VA-ECMO, their subsequent recovery, and if and how rehabilitation interventions may affect outcomes.

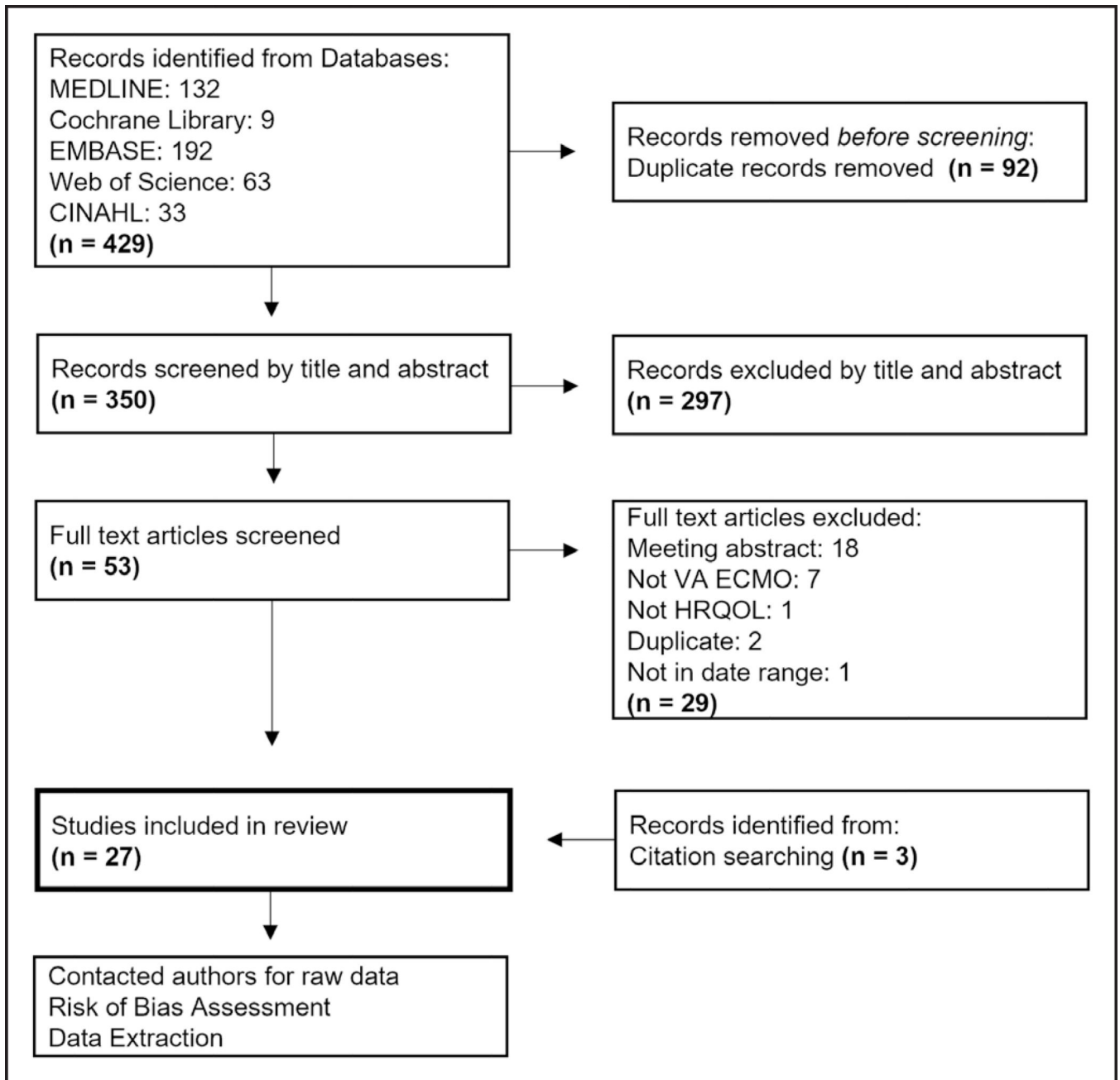


Figure 1. Flow diagram of methods. HRQOL = health-related quality of life, VA-ECMO = venoarterial extracorporeal membrane oxygenation.

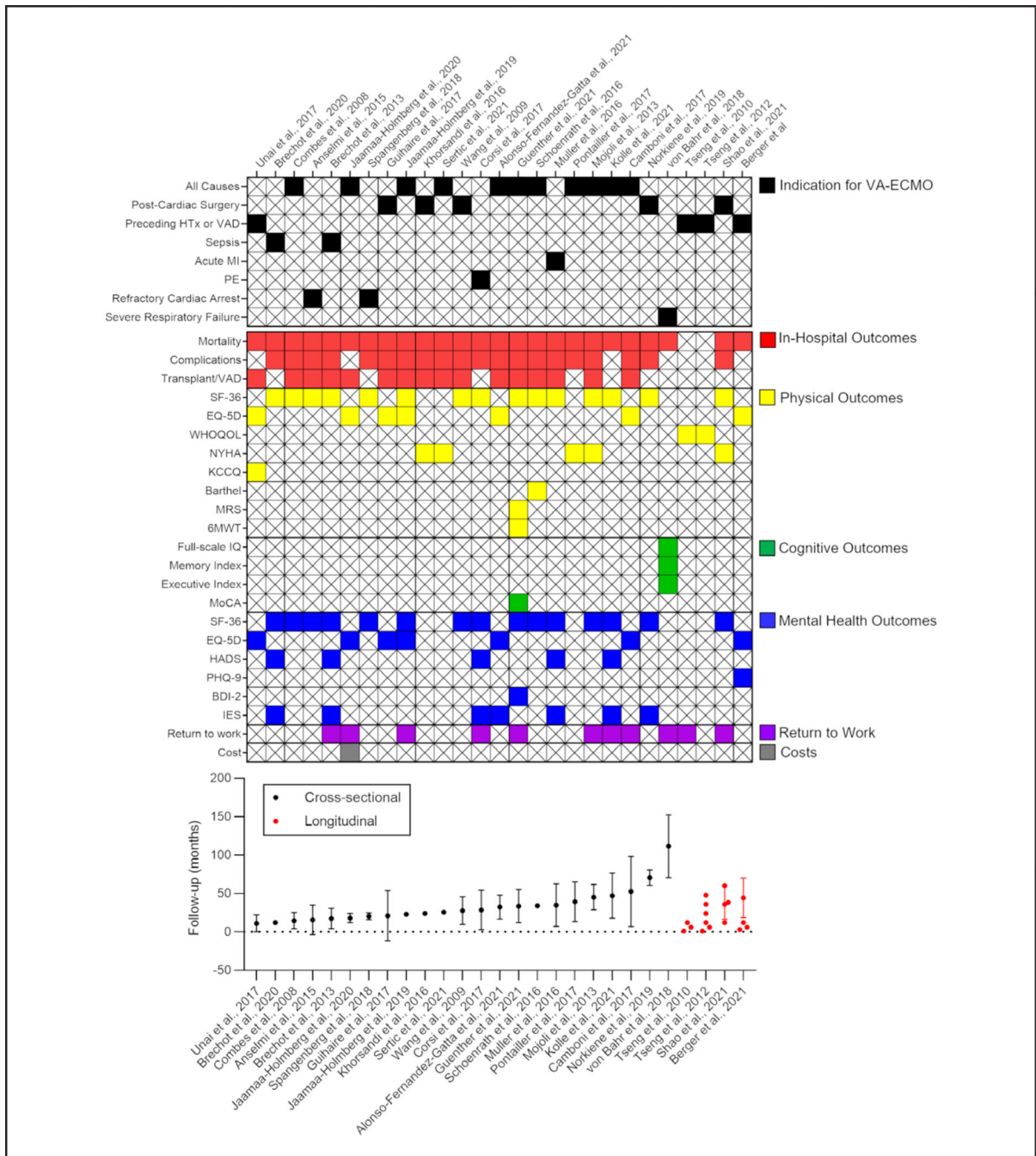


Figure 2. Summary of studies. The top panel is a graphical representation of the indication for VA-ECMO and what instrument was used to evaluate in-hospital, physical cognitive, and mental health outcomes, and whether the study reported return to work or healthcare costs. The bottom panel provides follow-up timepoints for cross-sectional and longitudinal studies. BDI-II = Beck Depression Inventory, second edition, EQ-5D = EuroQOL 5-dimension questionnaire, HADS = Hospital Anxiety and Depression Scale, HTx = heart transplant, IES-R = Impact of Event Scale, Revised, KCCQ = Kansas City

Cardiomyopathy Questionnaire, MoCA = Montreal Cognitive Assessment, NYHA = New York Heart Association, PF = physical functioning, PHQ-9 = patient health questionnaire 9, SF-36 = Short Form 36-Item Health Survey, VAD = ventricular assist device, VA-ECMO = venoarterial extracorporeal membrane oxygenation, WHOQOL = World Health Organization QOL.

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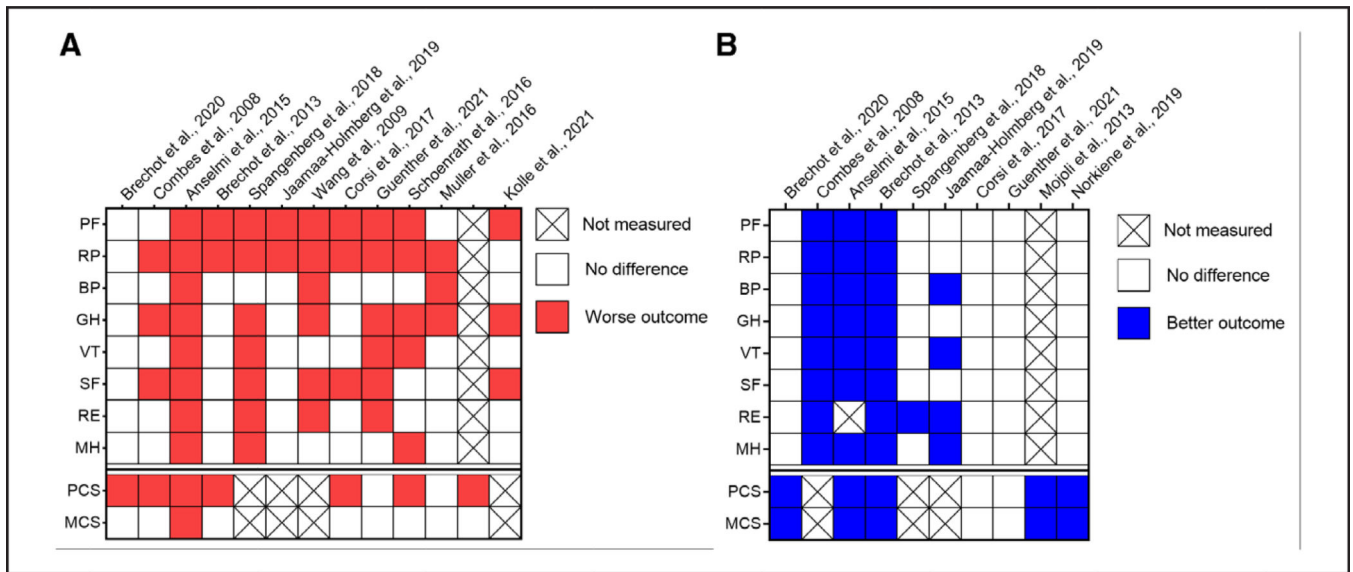


Figure 3. Summary of Short Form 36-Item Health Survey (SF-36) data. Summary of SF-36 data for venoarterial extracorporeal membrane oxygenation (VA-ECMO) Survivors compared with the General Population (**A**) or Individuals with Chronic Disease (**B**). SF-36 Domains: physical functioning (PF), role limitations due to physical health problems (RP), role limitation due to emotional problems (RE), social functioning (SF), bodily pain (BP), energy/fatigue or vitality (VT), emotional well-being or mental health (MH), and general health perceptions (GH). SF-36 Summary Scores: physical component summary (PCS) and mental component summary (MCS).

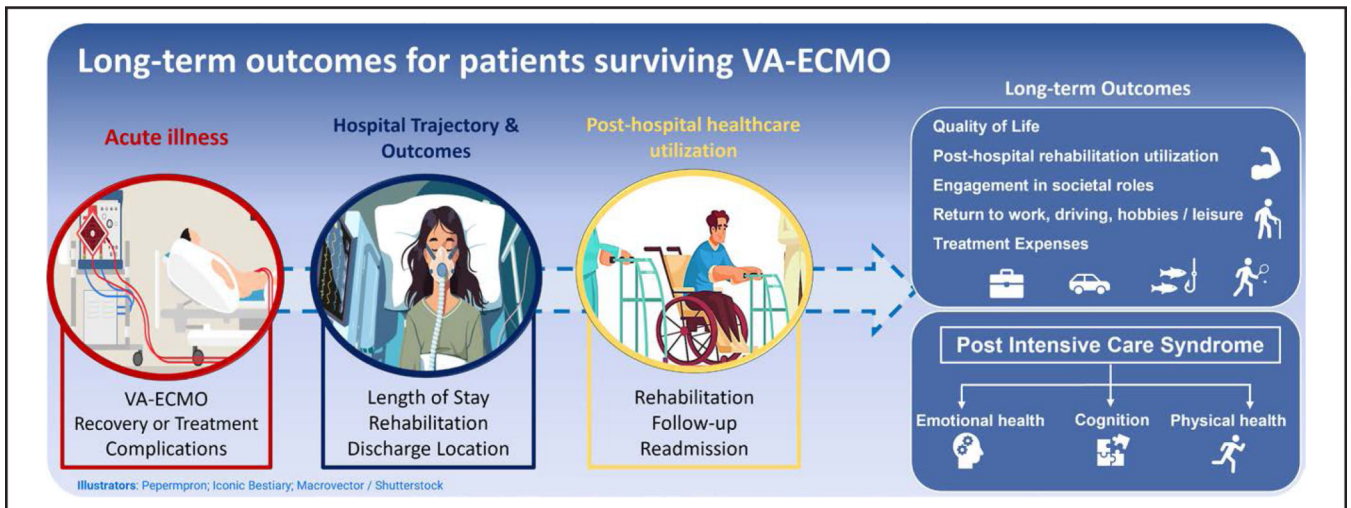


Figure 4. Long-term outcomes for patients surviving venoarterial extracorporeal membrane oxygenation (VA-ECMO). Future studies evaluating the long-term outcomes of patients surviving VA-ECMO should consider the indications for VA-ECMO and in-hospital outcomes in addition to short-term posthospital utilization and long-term outcomes (6). VA-ECMO = venoarterial extracorporeal membrane oxygenation.

TABLE 1.

Summary of Outcomes Related to PICS

PICS Domain	Instrument	Outcome	No. of Studies	n, VA-ECMO survivors	Pooled Mean Follow-up Time (mo)
Physical	LVEF (mean ± SD)	52.3 ± 11.1%	6	169	25 ± 12
	6 MWD, % predicted, median (IQR)	68.8 (61.7–91.6)	1	21	34 ± 22
	NYHA functional status	88% class I or II	7	162	30 ± 18
	Barthel Index	98/100	1	16	34
	mRS	94% 2 (free from moderate/severe disability)	1	36	34 ± 22
	IADLs	28% moderate limitations in IADLs	1	7	29 ± 26
	SF-36 PF ^a (mean ± SD)	71.1 ± 14.3	13	311	26.4 ± 13.4
	SF-36 RP ^a (mean ± SD)	53.7 ± 26.2	13	311	26.4 ± 13.4
	SF-36 BP ^a (mean ± SD)	75.4 ± 14.2	13	311	26.4 ± 13.4
	SF-36 GH ^a (mean ± SD)	59.1 ± 10.7	13	311	26.4 ± 13.4
Mental health	HAD-A	35% significant/severe symptoms of anxiety	5	109	29 ± 18
	HAD-D/PHQ-9/BDI-II	26% of symptoms of depression	7	152	30 ± 19
	IES	21% at risk for PTSD	7	158	33 ± 18
	SF-36 VT ^a (mean ± SD)	57.6 ± 11.8	13	311	26.4 ± 13.4
	SF-36 SF ^a (mean ± SD)	75.5 ± 15.2	13	311	26.4 ± 13.4
	SF-36 RE ^a (mean ± SD)	69.8 ± 21.0	13	311	26.4 ± 13.4
	SF-36 MH ^a (mean ± SD)	69.9 ± 9.4	13	311	26.4 ± 13.4
	FSIQ	92 ± 12	1	28	112 ± 41
	Memory Index	97 ± 13	1	28	112 ± 41
	Executive Index	97 ± 11	1	28	112 ± 41
Other	MoCA, median (IQR)	26.0 (22.5–28.0)	1	36	34 ± 22
	Return to work	19–57%	10	392	40 ± 22
	Sleep disturbance	71.40%	1	20	36
Intervention	Rehabilitation, discharge to follow-up	97%	1	79	34 ± 22
	Psychologic intervention	50%	1	10	17 ± 13

FSIQ = full-scale intelligence quotient, HADS = Hospital Anxiety and Depression Scale, IADL = instrumental activities of daily living, IES-R = Impact of Event Scale, Revised, IQR = interquartile range, LVEF = left ventricular ejection fraction, MH = emotional well-being or mental health, MoCA = Montreal Cognitive Assessment, mRS = Modified Rankin Scale, NYHA = New York Heart Association,

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PF = physical functioning, PHQ-9 = patient health questionnaire 9, PICS = postintensive care syndrome, PTSD = posttraumatic stress disorder, RE = role limitation due to emotional problems, RP = role limitations due to physical health problems, SF = social functioning, SF-36 = Short Form 36-Item Health Survey, VT = energy/fatigue or vitality.

^aSF-36 Domains: PF, RP, RE, SF, BP, VT, MH, GH.