Ten-year territory-wide trends in the utilisation and clinical outcomes of extracorporeal membrane oxygenation in Hong Kong

Pauline Y Ng *, Vindy WS Chan, April Ip, Lowell Ling, KM Chan, Anne KH Leung, Kenny KC Chan, Dominic So, HP Shum, CW Ngai, WM Chan, WC Sin

ABSTRACT

Introduction: The utilisation of extracorporeal membrane oxygenation (ECMO) has been rapidly increasing in Hong Kong. This study examined 10-year trends in the utilisation and clinical outcomes of ECMO in Hong Kong.

Methods: We retrospectively reviewed the records of all adult patients receiving ECMO who were admitted to the intensive care units (ICUs) of public hospitals in Hong Kong between 2010 and 2019. Temporal trends across years were assessed using the Mann–Kendall test. Observed hospital mortality was compared with the Acute Physiology and Chronic Health Evaluation (APACHE) IV–predicted mortality.

Results: The annual number of patients receiving ECMO increased from 18 to 171 over 10 years. In total, 911 patients received ECMO during the study period: 297 (32.6%) received veno-arterial ECMO, 450 (49.4%) received veno-venous ECMO, and 164 (18.0%) received extracorporeal cardiopulmonary resuscitation. The annual number of patients aged ≥65 years increased from 0 to 47 (27.5%) [P for trend=0.001]. The median (interquartile range) Charlson Comorbidity Index increased from 1 (0-1) to 2 (1-3) [P for trend<0.001] while the median (interquartile range) APACHE IV score increased from 90 (57-112) to 105 (77-137) [P for trend=0.003]. The overall standardised mortality ratio comparing hospital mortality with APACHE IV–predicted mortality was 1.11 (95% confidence interval=1.01-1.22). Hospital and ICU length of stay both significantly decreased (P for trend=0.011 and <0.001, respectively).

Conclusion: As ECMO utilisation increased in Hong Kong, patients put on ECMO were older, more critically ill, and had more co-morbidities. It is important to combine service expansion with adequate resource allocation and training to maintain quality of care.

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New knowledge added by this study

- During the 10-year study period, there was increasing utilisation of extracorporeal membrane oxygenation (ECMO) in older patients, patients with more co-morbidities, and patients with greater disease severity.
- Patients receiving ECMO require significant resources for out-of-hours services, inter-hospital transfers, and major operations.
- Although the observed hospital mortality was comparable with the Acute Physiology and Chronic Health Evaluation IV–predicted mortality, efforts should be made to systematically collect physiological data for computation of Survival after Veno-Arterial ECMO and Respiratory ECMO Survival Prediction scores in the future.

Implications for clinical practice or policy

- Among patients receiving ECMO in Hong Kong, clinical outcomes can be improved by revising patient selection criteria, enhancing therapy for bridge to transplantation and promoting organ transplantation, and consolidating ECMO services in specialised centres.

香港體外膜氧合使用和臨床結果的十年趨勢

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引言：體外膜氧合的使用在香港迅速普及。本研究探討香港體外膜氧合使用和臨床結果的十年趨勢。

方法：我們對2010至2019年間入住香港公立醫院深切治療部的體外膜氧合成年患者紀錄進行了回顧性分析。我們使用Mann–Kendall趨勢檢驗法分析該十年間的時間性趨勢，並將觀察到的醫院死亡率與急性生理和慢性健康評分IV（APACHE IV）所預測的死亡率進行比較。

結果：每年接受體外膜氧合治療的患者數目在十年間由18名增加至171名。研究期間共有911名患者接受體外膜氧合治療，當中297名（32.6%）接受靜脈至動脈體外膜氧合治療，450名（49.4%）接受靜脈至靜脈體外膜氧合治療，及164名（18.0%）使用體外膜氧合輔助心肺復甦。每年的65歲或以上的患者由0增加至47名（27.5%）[趨勢性分析P值=0.001]。查爾森合併症指數的中位數值（四分位數間距）由1（0-1）增加至2（1-3）[趨勢性分析P值<0.001]，而APACHE IV評分的中位數值（四分位數間距）則由90（57-112）增加至105（77-137）[趨勢性分析P值=0.003]。比較醫院死亡率及APACHE IV所預測的死亡率的整體標準化死亡比為1.11（95%置信區間=1.01-1.22）。住院日數及留醫深切治療部日數均明顯下降（趨勢性分析P值分別為0.011及<0.001）。

結論：隨着體外膜氧合的使用在香港愈趨普及，接受體外膜氧合治療的患者年紀較大、病情較危重及有較多合併症。擴展服務、確保資源分配足夠及培訓充足對保持照護質素十分重要。

Introduction

Extracorporeal membrane oxygenation (ECMO) offers life-sustaining support by supplementing heart and lung functions in patients with circulatory or respiratory failure. There is increasing utilisation of ECMO in intensive care units (ICUs) worldwide; for example, the Extracorporeal Life Support Organization (ELSO) registry reported a 10-fold increase in ECMO runs from 1643 in 1990 to 18 260 in 2020.[1] Hong Kong is a Special Administrative Region of the People's Republic of China, with a population of 7.4 million and an independent healthcare system.[2] In Hong Kong, various assessments of ICU performance have been performed for other disease entities,[3] but there have been few reports of ECMO-specific data and patient outcomes.[4] In particular, Hong Kong has a higher ECMO centre–to-population ratio compared with international guidelines.[5,6] A retrospective study examined the risk score–mortality association in patients receiving ECMO, but it only included data from a single tertiary ICU and was not fully representative of territory-wide practices.[7] Because ECMO is a high-cost, labour-intensive ICU treatment modality, it is important to understand how ECMO is utilised in Hong Kong, its associated resource implications, and review patient outcomes for future planning efforts.

In this study, using a territory-wide administrative registry of all patients receiving ECMO in the ICUs of public hospitals in Hong Kong, we examined trends in ECMO utilisation and clinical outcomes. Our primary objective was to summarise the status of ECMO services in Hong Kong over the past decade.

Methods

Study population

This retrospective observational study covered the period from 1 January 2010 to 31 December 2019. All adult patients aged ≥18 years with an ECMO episode and admission to the ICU of a public hospital under the Hospital Authority were identified using an administrative ECMO patient registry managed by a centralised ICU committee. An episode of ECMO was defined on the basis of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) procedure code for ECMO.[8] The need for ICU admission was determined using the Acute Physiology and Chronic Health Evaluation IV (APACHE IV) evaluation form.[9,10] Patients with missing ECMO details (eg, ECMO duration and configuration) and patients managed in non-mixed disciplinary ICUs were excluded from the study.

Data collection

Extracorporeal membrane oxygenation data were extracted from the administrative patient registry, which contained information about ECMO configuration, time of initiation, and time of discontinuation that had been entered by qualified nurses at the corresponding ECMO centre. The Clinical Data Analysis and Reporting System (CDARS), a central de-identified data repository comprising electronic health records from all public hospitals in Hong Kong, was accessed to collect patient baseline characteristics and components of the following disease severity scores: Sequential Organ Failure Assessment (SOFA),[11] Survival after Veno-Arterial ECMO (SAVE),[12] Respiratory ECMO Survival Prediction (RESP),[13] Charlson Comorbidity Index (CCI), and APACHE IV[14] (online supplementary Table 1). For patients with multiple ICU admissions during a single hospital stay, the APACHE IV score for the first ICU admission was used. Clinical outcomes including length of stay (LOS) and mortality were retrieved from the CDARS.

Study outcomes and definitions

The primary outcomes were trends in ECMO utilisation over 10 years, including number of patients receiving ECMO, illness severity (as measured by disease severity scores), and numbers of tertiary and quaternary inter-hospital transfers. Secondary outcomes were mortality, hospital and ICU LOS, transplantation procedures, ventricular assistive device (VAD) implantation, and complications. For patients who were transferred between hospitals, hospital mortality was defined as death during the final hospitalisation. Four common complications of ECMO, namely haemorrhagic, neurological, renal and cardiovascular complications, were identified using ICD-9-CM diagnostic and procedural codes (online supplementary Table 2).[8] Major non-cranial bleeding was identified as the diagnosis of gastrointestinal, major internal, and/or postoperative bleeding; alternatively, it was identified by the need for haemostatic procedures, transfusion of >2 units of packed red blood cells over 24 hours, and/or use of recombinant factor VII. Stroke was subdivided into haemorrhagic and ischaemic types. Patients with acute ischaemic limbs were identified by the diagnosis of acute limb ischaemia or compartment syndrome or by the performance of limb-saving procedures (eg, fasciotomy and amputation). Brain death was identified by the appropriate diagnostic code or by a procedure code indicating organ collection from a deceased donor.

For the purposes of subsequent analyses, ECMO centres referred to designated ICUs under the governance of the Hospital Authority Central Organising Committee in ICU Services. An emergency admission was defined as an admission in which the patient had emergency room attendance records within the preceding 12 hours. Extracorporeal membrane oxygenation initiation in the emergency room was defined as an ECMO episode in which the patient had emergency room attendance records within the preceding 24 hours. An inter-hospital transfer was defined when ECMO was started at another institution before patient transferal with ECMO in situ to one of six ECMO centres. A transfer to a quaternary cardiothoracic unit was defined as an instance of intra- or inter-hospital transfer from a mixed ICU to cardiothoracic care in one of three centres, either during ECMO care or within 12 hours after stopping ECMO.

Statistical analysis

Frequencies and percentages were used to describe categorical variables. The Shapiro–Wilk test was used to assess data normality; data were expressed as means with standard deviations or medians with interquartile ranges, as appropriate. Categorical variables were compared between groups using the Chi squared test; continuous variables were compared by the *t* test or Mann-Whitney *U* test, as appropriate. The Mann–Kendall test was used to assess temporal trends in patient characteristics and outcomes across years, in sequential order from 2010 to 2019. Model discrimination and model calibration of risk scores in predicting hospital mortality were examined using the area under the receiver operating characteristic (AUROC) curve and the Hosmer–Lemeshow test. The observed hospital mortality was compared with that predicted from risk scores using standardised mortality ratios (SMRs). Patients with missing APACHE IV scores were excluded from this analysis.

All statistical analysis and data visualisation procedures were performed in Stata 16 (StataCorp; College Station [TX], United States). Tests were considered statistically significant when two-tailed P values were <0.05.

Results

Patient characteristics and co-morbidities

From January 2010 to December 2019, among 125 101 ICU admissions overall in Hong Kong, 911 (0.73%) involved patients receiving ECMO as follows: 297 (32.6%) veno-arterial (V-A) ECMO, 450 (49.4%) veno-venous (V-V) ECMO, and 164 (18.0%) extracorporeal cardiopulmonary resuscitation (ECPR) [Fig 1]. There was a steady increase in the annual number of patients receiving ECMO, with a 9.5-fold increase from 18 episodes in 2010 to 171 episodes in 2019 (Fig 2). The annual number of V-A ECMO episodes significantly increased from 3 (16.7%) to 67 (39.2%) over 10 years (P for trend=0.001) [Table 1]. The total number of ECMO patient-days increased from 109 in 2010 to 1565 in 2019 (online supplementary Fig 1).

A total of 583 (64.0%) patients were male, with a median age at admission of 54 years (interquartile range, 42-62), and 185 (20.3%) patients of ≥65 years. There was increasing utilisation of ECMO among patients aged ≥65 years (P for trend=0.001). The median CCI was 1 (0-2), and an increasing number of patients had a CCI ≥2 (P for trend=0.002) [Table 1].

Among the 889 (97.6%) patients with complete APACHE IV data, the median APACHE IV score was 100 (73-132), with an increase from 90 (57-112) in 2010 to 105 (77-137) in 2019 (P for trend=0.003); the median APACHE IV–estimated risk of death was 0.5 (0.2-0.8). Complete demographic details are shown in Table 1; trends in co-morbidities and disease severity scores are shown in online supplementary Figure 2.

Extracorporeal membrane oxygenation resources and inter-hospital transfers

Within the publicly funded hospital system, the number of ECMO centres under centralised ICU governance increased from three in 2010 to five in 2015, and then seven in 2019. The total number of available ECMO consoles paralleled the increase: from three in 2010 to nine in 2015, and then 11 in 2019 (online supplementary Table 3).

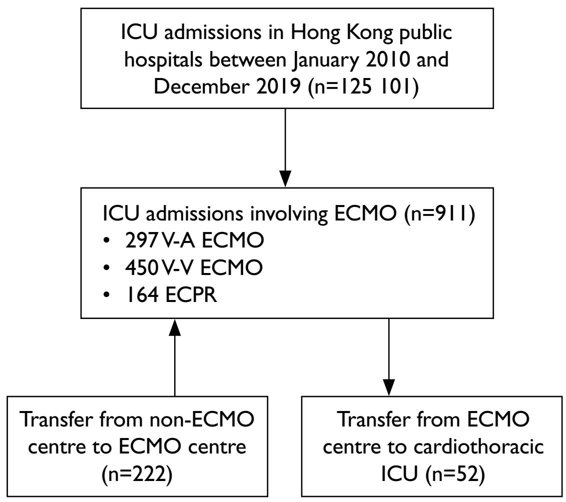

FIG 1. Study cohort
Abbreviations: ECMO = extracorporeal membrane oxygenation; ECPR = extracorporeal cardiopulmonary resuscitation; ICU = intensive care unit; V-A = veno-arterial; V-V = veno-venous

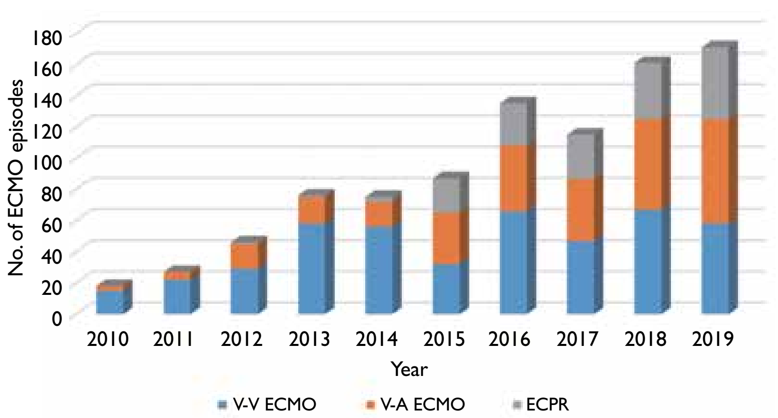

FIG 2. Numbers and types of extracorporeal membrane oxygenation (ECMO) episodes from 2010 to 2019
Abbreviations: ECPR = extracorporeal cardiopulmonary; V-A = veno-arterial; V-V = veno-venous

Among the 911 patients receiving ECMO, 469 (51.5%) were initiated outside of the regular 9 am to 5 pm period, including 247 (52.7%) patients receiving V-V ECMO, 137 (29.2%) patients receiving V-A ECMO, and 85 (18.1%) patients receiving ECPR. In total, 710 (77.9%) emergency admissions were identified. These patients were younger, had fewer co-morbidities, and were more likely to receive V-V ECMO [371/710 (52.3%) vs 79/201 (39.3%); P=0.001]. In total, 370 (40.6%) patients had ECMO initiated within 24 hours of emergency admission; these patients were more likely to receive ECPR [113/370 (30.5%) vs 51/541 (9.4%); P<0.001] and have higher APACHE IV scores [118 (86-146) vs 91 (69-118); P<0.001].

Overall, there were 222 (24.4%) episodes of inter-hospital transfer from non-ECMO centres to ECMO centres; the annual number of episodes increased from one (1/18 [5.6%]) in 2010 to 22 (22/171 [12.9%]) in 2019 (P for trend<0.001) [online supplementary Fig 3]. In total, 173 (77.9%) patients were transferred from ICUs in other hospitals; the remaining 49 patients were transferred from non-ICU settings. Most transferred patients (66.2%) received V-V ECMO (online supplementary Fig 4a); their principal diagnoses are shown in online supplementary Figure 4b and 4c. Transferred patients had worse RESP scores [-2 (-4 to 0) vs -1 (-3 to 2); P<0.001], better SAVE scores (-6 ± 5 vs -8 ± 5; P=0.012), and lower APACHE IV scores [89 (69-117) vs 104 (75-136); P<0.001]. Among the patients transferred to ECMO centres, 54 (24.3%) underwent a major operation within 7 days of transfer, and 32 (59.3%) of these surgeries involved the cardiovascular system. Other procedural details are shown in online supplementary Figure 4d and 4e.

There were 52 (5.7%) episodes of inter-hospital transfer to quaternary cardiothoracic ICUs; the annual number remained relatively consistent throughout the 10-year study period (P for trend=0.121) [online supplementary Fig 3]. Patients in these transfers were younger (P=0.048); they were more likely to receive V-A ECMO [31/52 (59.6%) vs 266/859 (31.0%); P<0.001] and ECPR [15/52 (28.8%) vs 149/859 (17.3%); P=0.036] (online supplementary Fig 5a). The primary diagnoses are shown in online supplementary Figure 5b and 5c. Among the patients involved in quaternary transfers, 22 (42.3%) underwent a major operation within 28 days of transfer, and 18 (81.8%) of these surgeries involved the cardiovascular system. Other procedural details are shown in online supplementary Figure 5d and 5e.

Patient outcomes

The overall numbers of hospital mortalities and ICU mortalities were 456 (50.1%) and 382 (41.9%), respectively. The numbers of hospital mortalities among patients receiving V-V ECMO, V-A ECMO, and ECPR were 152 (33.9%), 178 (59.9%), and 126 (76.8%), respectively (online supplementary Table 4). The median hospital LOS was 26.8 (interquartile range, 10.7-55.6) days, and the median ICU LOS was 10.2 (interquartile range, 4.8-20.1) days [Table 2]. Throughout the 10-year study period, the annual number of hospital mortalities increased from one (5.6%) in 2010 to 90 (52.6%) in 2019 (P for trend<0.001). The hospital LOS decreased from 36.6 (interquartile range, 26.8-57.2) to 25.2 (7.6-50.2) days [P for trend=0.011], and ICU LOS decreased from 15.5 (10.8-18.2) days in 2010 to 7.9 (3.9-19.8) days in 2019 (P for trend<0.001).

TABLE 1. Demographic characteristics of patients receiving extracorporeal membrane oxygenation (ECMO) from 2010 to 2019 in Hong Kong (n=911)*

	Year										P for trend
	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	
No. of ECMO episodes	18	27	46	75	75	87	135	116	161	171	
Basic demographics											
Age at admission, y	42 (34-51)	50 (39-59)	52 (39-59)	53 (38-61)	55 (42-61)	54 (41-64)	55 (39-63)	56 (46-62)	54 (43-62)	57 (47-65)	<0.001
Age ≥65 y	0	3 (11.1%)	5 (10.9%)	11 (14.7%)	14 (18.7%)	21 (24.1%)	29 (21.5%)	24 (20.7%)	31 (19.3%)	47 (27.5%)	0.001
Male sex	9 (50.0%)	18 (66.7%)	34 (73.9%)	34 (45.3%)	40 (53.3%)	56 (64.4%)	85 (63.0%)	77 (66.4%)	105 (65.2%)	125 (73.1%)	0.003
ECMO patient-days	109	204	366	751	896	799	1287	1299	1210	1565	<0.001
Type of ECMO											
V-A ECMO	3 (16.7%)	5 (18.5%)	16 (34.8%)	16 (21.3%)	16 (21.3%)	33 (37.9%)	42 (31.1%)	41 (35.3%)	58 (36.0%)	67 (39.2%)	0.001
V-V ECMO	15 (83.3%)	22 (81.5%)	29 (63.0%)	58 (77.3%)	56 (74.7%)	32 (36.8%)	66 (48.9%)	47 (40.5%)	67 (41.6%)	58 (33.9%)	<0.001
ECPR	0	0	1 (2.2%)	1 (1.3%)	3 (4.0%)	22 (25.3%)	27 (20.0%)	28 (24.1%)	36 (22.4%)	46 (26.9%)	<0.001
Type of ICU admission											
Elective postoperation	1 (5.6%)	0	1 (2.2%)	1 (1.3%)	1 (1.3%)	3 (3.4%)	7 (5.2%)	5 (4.3%)	8 (5.0%)	2 (1.2%)	0.59
Emergency postoperation	1 (5.6%)	2 (7.4%)	1 (2.2%)	1 (1.3%)	6 (8.0%)	6 (6.9%)	6 (4.4%)	6 (5.2%)	12 (7.5%)	7 (4.1%)	0.68
Medical	16 (88.9%)	25 (92.6%)	44 (95.7%)	73 (97.3%)	68 (90.7%)	78 (89.7%)	122 (90.4%)	105 (90.5%)	141 (87.6%)	162 (94.7%)	0.50
Type of hospital admission											
Emergency	11 (61.1%)	19 (70.4%)	33 (71.7%)	58 (77.3%)	58 (77.3%)	66 (75.9%)	91 (67.4%)	90 (77.6%)	115 (71.4%)	130 (76.0%)	0.64
Principle diagnoses											
V-A ECMO											
Ischaemic heart disease	0	0	1 (2.2%)	3 (4.0%)	3 (4.0%)	7 (8.0%)	10 (7.4%)	16 (13.8%)	6 (3.7%)	19 (11.1%)	0.004
Heart failure	1 (5.6%)	1 (3.7%)	2 (4.3%)	3 (4.0%)	1 (1.3%)	5 (5.7%)	4 (3.0%)	3 (2.6%)	5 (3.1%)	9 (5.3%)	0.85
Pulmonary embolism	0	0	0	0	0	3 (3.4%)	0	0	1 (0.6%)	3 (1.8%)	0.24
Valvular heart disease	0	1 (3.7%)	1 (2.2%)	1 (1.3%)	1 (1.3%)	4 (4.6%)	4 (3.0%)	3 (2.6%)	10 (6.2%)	7 (4.1%)	0.08
Myocarditis	1 (5.6%)	1 (3.7%)	7 (15.2%)	2 (2.7%)	6 (8.0%)	5 (5.7%)	8 (5.9%)	8 (6.9%)	9 (5.6%)	3 (1.8%)	0.07
Aortic dissection	0	0	0	0	1 (1.3%)	1 (1.1%)	3 (2.2%)	1 (0.9%)	6 (3.7%)	3 (1.8%)	0.055
Cardiac tamponade	0	0	0	0	0	0	0	0	2 (1.2%)	2 (1.2%)	0.046
Arrhythmia	0	1 (3.7%)	0	0	0	0	0	0	1 (0.6%)	2 (1.2%)	0.58
Pneumonia	0	0	1 (2.2%)	1 (1.3%)	1 (1.3%)	0	2 (1.5%)	0	5 (3.1%)	7 (4.1%)	0.036
Others: V-A	1 (5.6%)	1 (3.7%)	4 (8.7%)	7 (9.3%)	3 (4.0%)	8 (9.2%)	11 (8.1%)	9 (7.8%)	13 (8.1%)	12 (7.0%)	0.83

Abbreviations: APACHE IV = Acute Physiology and Chronic Health Evaluation IV; CCI = Charlson Comorbidity Index; ECPR = extracorporeal cardiopulmonary resuscitation; ICU = intensive care unit; RESP = Respiratory ECMO Survival Prediction; SAVE = Survival after Veno-Arterial ECMO; SOFA = Sequential Organ Failure Assessment; V-A = veno-arterial; V-V = veno-venous

* Data are presented as No. (%), mean ± standard deviation or median (interquartile range), unless otherwise specified

† Calculated using documented co-morbidities before hospital admission

‡ Calculated using components collected within 24 hours of ICU admission

§ Calculated using components collected within 24 hours of ECMO initiation

‖ Calculated for patients receiving V-A ECMO only

¶ Calculated for patients receiving V-V ECMO only

** 22 (2.4%) patients were excluded from the calculation because of missing data in one or more APACHE components; therefore, n=889

TABLE 1. (cont'd)

	Year										P for trend
	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	
V-V ECMO											
Viral pneumonia	8 (44.4%)	5 (18.5%)	1 (2.2%)	10 (13.3%)	20 (26.7%)	5 (5.7%)	21 (15.6%)	4 (3.4%)	13 (8.1%)	18 (10.5%)	0.001
Bacterial pneumonia	6 (33.3%)	8 (29.6%)	16 (34.8%)	18 (24.0%)	22 (29.3%)	16 (18.4%)	29 (21.5%)	21 (18.1%)	29 (18.0%)	25 (14.6%)	<0.001
Asthma	0	0	0	1 (1.3%)	0	0	1 (0.7%)	5 (4.3%)	1 (0.6%)	0	0.62
Others: V-V	1 (5.6%)	9 (33.3%)	12 (26.1%)	29 (38.7%)	14 (18.7%)	11 (12.6%)	15 (11.1%)	17 (14.7%)	24 (14.9%)	15 (8.8%)	<0.001
ECPR											
Ischaemic heart disease	0	0	0	1 (1.3%)	0	7 (8.0%)	8 (5.9%)	8 (6.9%)	11 (6.8%)	14 (8.2%)	<0.001
Heart failure	0	0	0	0	0	0	3 (2.2%)	1 (0.9%)	1 (0.6%)	1 (0.6%)	0.35
Pulmonary embolism	0	0	0	0	0	0	1 (0.7%)	0	1 (0.6%)	7 (4.1%)	0.002
Valvular heart disease	0	0	0	0	0	2 (2.3%)	0	1 (0.9%)	0	3 (1.8%)	0.20
Myocarditis	0	0	0	0	1 (1.3%)	3 (3.4%)	1 (0.7%)	2 (1.7%)	1 (0.6%)	5 (2.9%)	0.13
Cardiac tamponade	0	0	0	0	1 (1.3%)	0	0	2 (1.7%)	1 (0.6%)	0	0.72
Sepsis	0	0	0	0	0	1 (1.1%)	0	3 (2.6%)	2 (1.2%)	1 (0.6%)	0.19
Others: ECPR	0	0	1 (2.2%)	0	1 (1.3%)	9 (10.3%)	14 (10.4%)	11 (9.5%)	19 (11.8%)	15 (8.8%)	<0.001
Predictive scores during ECMO episodes											
CCI[†]	1 (0-1)	1 (0-2)	1 (0-2)	1 (0-2)	1 (0-2)	2 (0-3)	1 (0-2)	2 (1-2)	1 (0-2)	2 (1-3)	<0.001
CCI ≥2	0	6 (22.2%)	10 (21.7%)	11 (14.7%)	14 (18.7%)	26 (29.9%)	29 (21.5%)	25 (21.6%)	38 (23.6%)	56 (32.7%)	0.002
SOFA on ICU[‡]	7 ± 3	8 ± 3	10 ± 4	8 ± 4	10 ± 4	11 ± 4	10 ± 4	11 ± 4	11 ± 4	12 ± 4	<0.001
SOFA on ECMO[§]	8 ± 3	9 ± 2	10 ± 3	9 ± 4	10 ± 3	9 ± 3	9 ± 3	9 ± 3	9 ± 4	9 ± 3	0.58
SAVE score[‖]	4 ± 4	-9 ± 3	-6 ± 5	-5 ± 5	-7 ± 5	-7 ± 5	-7 ± 4	-8 ± 4	-8 ± 5	-9 ± 5	<0.001
RESP score[¶]	-1 (-3 to 1)	-1 (-3 to 2)	-1 (-3 to 1)	-1 (-3 to 2)	-1 (-3 to 2)	-1 (-3 to 1)	-2 (-3 to 1)	-1 (-4 to 1)	-1 (-4 to 1)	-1 (-3 to 0)	0.46
No. of APACHE IV patients**	16 (88.9%)	27 (100%)	46 (100%)	70 (93.3%)	73 (97.3%)	87 (100%)	133 (98.5%)	113 (97.4%)	154 (95.7%)	170 (99.4%)	0.27
APACHE IV score	90 (57-112)	84 (62-109)	99 (72-127)	83 (71-119)	100 (73-132)	105 (82-136)	99 (71-131)	103 (73-134)	103 (70-139)	105 (77-137)	0.003
APACHE IV–estimated hospital mortality	0.3 (0.1-0.7)	0.3 (0.2-0.5)	0.3 (0.2-0.7)	0.3 (0.2-0.7)	0.5 (0.2-0.8)	0.6 (0.3-0.9)	0.4 (0.2-0.8)	0.4 (0.2-0.8)	0.4 (0.2-0.9)	0.6 (0.3-0.9)	<0.001
APACHE IV–estimated length of stay	7.6 (6.8-8.1)	8.1 (7.2-9.2)	7.5 (5.6-9.2)	7.7 (6.4-8.7)	7.7 (6.0-8.6)	6.1 (4.2-8.2)	6.9 (4.4-8.9)	6.1 (4.3-8.0)	6.4 (4.4-8.4)	6.3 (4.3-8.4)	<0.001

After adjustments for age, sex, APACHE IV score, and type of ECMO, the odds of hospital mortality were significantly lower in patients with ECMO initiated within 24 hours of emergency admission (adjusted odds ratio [OR]=0.56, 95% confidence interval [CI]=0.40-0.78; P=0.001). There were no significant associations with hospital mortality among patients who had emergency admission (adjusted OR=0.78, 95% CI=0.54-1.12; P=0.17), patients who were transferred to ECMO centres (adjusted OR=0.74, 95% CI=0.52-1.05; P=0.09), or patients who were transferred to quaternary cardiothoracic ICUs (adjusted OR=0.58, 95% CI=0.30-1.13; P=0.11). Patients transferred to quaternary cardiothoracic ICUs had significantly lower ICU mortality [4 (7.7%) vs 378 (44.0%);

TABLE 2. Clinical outcomes among patients receiving extracorporeal membrane oxygenation (ECMO) from 2010 to 2019 in Hong Kong (n=911)*

	No. of events (%)
Outcomes	
Hospital mortality	456 (50.1%)
28-day mortality	359 (39.4%)
ICU mortality	382 (41.9%)
Hospital length of stay, d	26.8 (10.7-55.6)
ICU length of stay, d	10.2 (4.8-20.1)
ECMO duration, d	5.4 (2.7-9.4)
Inter-hospital transfer	
From non-ECMO centre to ECMO centre	222 (24.4%)
From ECMO centre to cardiothoracic ICU	52 (5.7%)
Complications†	
Major non-cranial bleeding	466 (51.2%)
Gastrointestinal haemorrhage	39 (4.3%)
Brain death	9 (1.0%)
Ischaemic limb	28 (3.1%)
Stroke	76 (8.3%)
Haemorrhagic	54 (5.9%)
Ischaemic or unclassified	22 (2.4%)
Renal replacement therapy required	39 (4.3%)
Cardiopulmonary resuscitation required	110 (12.1%)
Cardiac arrhythmia	64 (7.0%)
Tamponade	8 (0.9%)
Pneumothorax	34 (3.7%)
Hyperbilirubinemia	113 (12.4%)
Haemolysis	11 (1.2%)
Subsequent procedures	
Isolated LVAD implantation	8 (0.9%)
BiVAD implantation	24 (2.6%)
Heart transplantation	8 (0.9%)
Lung transplantation	1 (0.1%)

Abbreviations: BiVAD = biventricular assistive device; ICU = intensive care unit; LVAD = left ventricular assistive device

* Data are presented as No. (%) or median (interquartile range)

† Refer to online supplementary Table 2

P<0.001] and significantly longer hospital LOS [38.3 (22.1-111.0) vs 25.6 (9.4-53.1) days, P<0.001]. The unadjusted and adjusted outcomes in various patient subgroups are presented in online supplementary Table 5.

In total, 41 (4.5%) patients were successfully bridged to VAD or transplantation. Among 461 patients who were receiving V-A ECMO and ECPR, 31 (6.7%) patients underwent VAD implantation and eight (1.7%) patients underwent heart transplantation. Among 450 patients who were receiving V-V ECMO, one (0.2%) patient underwent lung transplantation.

In terms of complications, there were 466 (51.2%) cases of major bleeding, 28 (3.1%) ischaemic limb complications, and nine (1.0%) patients who were declared brain-dead. Among 76 (8.3%) patients with stroke, 54 (5.9%) had haemorrhagic stroke (Table 2).

Prediction of hospital mortality

The ability of risk scores to predict post-ECMO hospital mortality was examined. There was a significant increase in the annual median APACHE IV score from 90 (57-112) in 2010 to 105 (77-137) in 2019 (P for trend=0.003). The SOFA score on the first day of ICU admission and the SAVE score in patients receiving V-A ECMO also showed significant trends (P for trend<0.001). No significant trends were observed regarding the SOFA score on the first day of ECMO (P for trend=0.58) or the RESP score in patients receiving V-V ECMO (P for trend=0.46) [Table 1].

The APACHE IV score showed good discriminatory power and was well calibrated for the prediction of hospital mortality (AUROC=0.727; Hosmer–Lemeshow test P=0.356); as was SOFA score on the first day of ECMO (AUROC=0.670; Hosmer–Lemeshow test P=0.322) [Fig 3]. The overall SMR for hospital mortality compared with APACHE IV–predicted mortality was 1.11 (95% CI=1.01-1.22) and there was no significant trend over the 10-year study period (P for trend=0.135) [Fig 4]. The SAVE and RESP scores, estimated using data from electronic health records, displayed limited discriminatory power for the prediction of hospital mortality in patients receiving V-A and V-V ECMO (AUROC=0.604 and 0.527, respectively). The ROC curves for various risk prediction models are shown in Figure 3.

Discussion

To our knowledge, this is the first 10-year longitudinal study of the majority of patients receiving ECMO in Hong Kong; the results showed that the numbers of patients and complexities of medical conditions increased throughout the study period. Although patients receiving ECMO represent a small proportion of ICU patients overall, they require significant resource utilisation including out-of-hours services, inter-hospital transfers, and major operations. Comparisons with standardised risk scores suggested satisfactory performance based on the APACHE IV model, but the lack of complete and granular patient data precluded meaningful conclusions with respect to ECMO-specific risk scores.

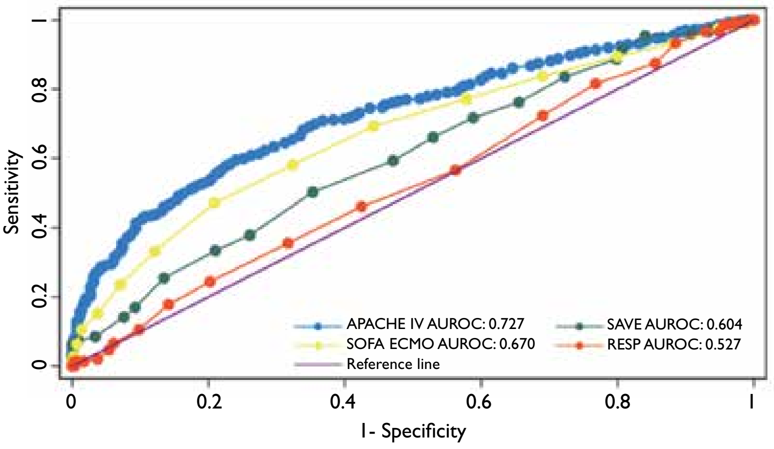

FIG 3. Receiver operating characteristic (ROC) curves for various risk prediction models

Abbreviations: APACHE IV = Acute Physiology and Chronic Health Evaluation IV; AUROC = area under the ROC curve; ECMO = extracorporeal membrane oxygenation; RESP = Respiratory ECMO Survival Prediction; SAVE = Survival after Veno-Arterial ECMO; SOFA = Sequential Organ Failure Assessment

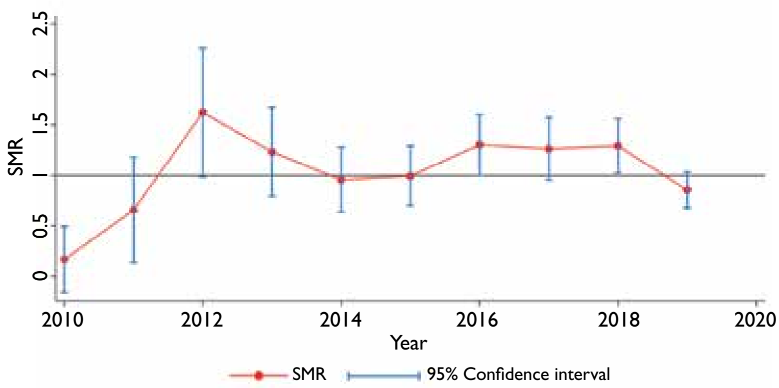

FIG 4. Standardised mortality ratio (SMR) for hospital mortality

Trends in patient characteristics

In addition to the observation of a 9.5-fold increase in ECMO utilisation in Hong Kong over the 10-year study period, including greater use of V-A ECMO after 2012 and rapid uptake of ECPR after 2015, this study revealed that patients receiving ECMO were increasingly older, had an increasing co-morbidity burden, and displayed greater disease severity upon ICU admission. This is not only attributable to the overall advances in ECMO,[15] but also encouraged by the multiple studies showing indistinguishable survival after ECMO in older adult patients compared with the younger ones.[16-18] The increased utilisation of ECMO in ECPR is supported by clinical trials demonstrating the efficacy of this approach. In the CHEER trial (mechanical CPR, Hypothermia, ECMO and Early Reperfusion), treatment with mechanical cardiopulmonary resuscitation, hypothermia, ECMO, and early reperfusion led to increased survival among patients with refractory cardiac arrest.[19] The ARREST trial (Advanced Reperfusion Strategies for Refractory Cardiac Arrest) showed a similar increase in survival upon initiation of early ECPR among patients with out-of-hospital cardiac arrest and refractory ventricular fibrillation.[20] The increasing numbers of patients receiving ECMO have also resulted from greater utilisation of V-A ECMO to manage conditions such as acute myocardial infarction complicated by refractory cardiogenic shock,[21] as well as efforts to transition to therapies including VAD and heart transplantation.[22] The overall growth of ECMO utilisation in Hong Kong is similar to global patterns evident in the ELSO registry.[1]

Patient mortality

The observed overall SMR for post-ECMO hospital mortality was slightly worse than the predicted overall SMR, possibly because ECMO services were in early phases of development at various centres throughout the study period. The decrease in SMR in the later portion of the study period, when ECMO services had matured at most centres, may be an indication of progress. When the results were stratified according to the type of ECMO, we found that the rate of hospital mortality among patients receiving V-V ECMO was better in Hong Kong than in the global ELSO registry (33.9% vs 40.8%), whereas the rates of hospital mortality among patients receiving V-A ECMO and ECPR were worse (V-A ECMO: 59.8% in Hong Kong vs 55.4% globally; ECPR: 76.8% in Hong Kong vs 69.8% globally). The sharp increase in ECPR utilisation may have contributed to an artificially elevated SMR, considering that ECPR is associated with worse survival relative to V-V ECMO and V-A ECMO[19]; notably, in a pilot cohort of patients receiving ECPR in Hong Kong, ICU survival was 32.4%.[23] The low rate of ECMO bridging to transplantation in Hong Kong—nine (1.0%) patients over 10 years—also reduces overall cohort survival. Among developed countries/regions, Hong Kong has a very low rate of registration in the Centralised Organ Donation Register (3.8%) and limited motivation to participate in organ donation.[24] Nevertheless, it remains important to actively explore methods to lower the SMR. One possibility involves consolidating ECMO services to a few specialised centres, based on evidence of a volume-outcome relationship repeatedly identified in other observational cohorts across various geographical regions and healthcare settings.[25,26] Furthermore, a study in the United States showed that multidisciplinary interventions—including coordination among surgeons, cardiologists, and ECMO specialists, as well as the implementation of standardised ECMO admission and weaning protocols—were associated with lower mortality in patients receiving ECMO,[27] indicating a need to strengthen interdisciplinary communication or expand collaborations with allied health services to maintain standards of care.

Risk prediction

The comparative utility of various risk scores for outcome prediction in Hong Kong merits attention. In terms of predicting hospital mortality among patients receiving ECMO in the present study, the APACHE IV score performed best, followed by the SOFA score on the first day of ECMO; the SAVE and RESP scores had moderate discriminatory power. The satisfactory performance of the APACHE IV score in Hong Kong was previously demonstrated in a large retrospective cohort study of ICU patients (c-statistic=0.889).[28] Importantly, most data were available for APACHE IV scores in the present study, and the corresponding accuracy was high. However, the main limitation of APACHE IV scores is the lack of definite correlation with the time and patient condition upon ECMO initiation,[29] which likely leads to a systemic under-representation of disease severity. The SOFA score, which can be calculated on a daily basis, has the theoretical advantage of more closely reflecting disease severity and clinical progression[30]; the SOFA score on the date of ECMO initiation demonstrated good performance in predicting hospital mortality among patients in our cohort. We note that the limited predictive performances of ECMO-specific SAVE and RESP scores are mainly related to the difficulty of retrieving accurate physiological data from the CDARS; various components of the scores were determined by a combination of diagnostic codes, procedural codes, and laboratory parameters. Although these scores have been validated in international cohorts,[12,13] their systematic adoption as benchmarks for ECMO service performance in Hong Kong is hindered by the lack of available patient data. Among the six ECMO centres included in the present study, only four routinely collect patient and ECMO data for submission to the international ELSO registry; none of the centres compute SAVE and RESP scores. Within the community of ECMO providers in Hong Kong, we strongly encourage collaborative efforts to routinely document ECMO-specific severity scores and improve coding practices within electronic health records and the CDARS; these approaches will facilitate outcome monitoring and resource allocation. Moreover, validation of these scores in Hong Kong will be informative because Asians were substantially underrepresented in the original score-development cohorts established using the ELSO international registry.[12,13]

Limitations

There were some limitations in this study. First, the retrospective observational design utilised data that were not recorded in a manner intended for research purposes; systematic biases in missing data may be present. Inaccurate diagnoses and procedural coding practices may have led to insufficient collection of relevant clinical data and information regarding ECMO circuit complications. However, the clinical outcomes of hospital mortality and LOS were captured from administrative data with a low risk of error. Second, the presence of between-centre heterogeneity related to non-uniform clinical practices may have contributed to outcome differences that were not reflected in the overall cohort. Third, patients receiving ECMO in non-mixed disciplinary ICUs or coronary care units were excluded from the study; outcomes and resource utilisation may have been considerably different among these patients. Finally, the collected data did not allow examination of ECMO cost-effectiveness, an important metric for service and resource planning.

Conclusion

In this territory-wide study, we observed increasing trends in ECMO utilisation in Hong Kong that were similar to global patterns. The overall observed mortality was reasonably close to the APACHE IV–predicted mortality. Systematic documentation of ECMO-specific risk scores is needed to ensure high-quality data for ECMO service benchmarking and development efforts.

Author contributions

Concept or design: PY Ng, A Ip.
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Drafting of the manuscript: PY Ng, VWS Chan.
Critical revision of the manuscript for important intellectual content: All authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

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Ethics approval

This research was approved by the Institutional Review Board of The University of Hong Kong/Hospital Authority Hong Kong West Cluster (Ref No.: UW 20-573). The research was conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived by the Board due to the retrospective nature of the research.

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