ปัญหาสุขภาพและผลลัพธ์ของการรักษาผู้ป่วยสูงอายุในหออภิบาลผู้ป่วยวิกฤตในประเทศที่มีรายได้น้อยและรายได้ปานกลาง: การทบทวนวรรณกรรมอย่างเป็นระบบและการวิเคราะห์อภิมาน

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บทคัดย่อ

ภูมิหลัง ผู้สูงอายุที่เข้ารับการรักษาในหออภิบาลผู้ป่วยวิกฤต (ไอซียู) มีอัตราตายสูง โดยเฉพาะในประเทศที่มีรายได้น้อยและรายได้ปานกลาง (LMICs)

วัตถุประสงค์ การวิจัยโดยการทบทวนวรรณกรรมอย่างเป็นระบบและการวิเคราะห์อภิมานนี้มีวัตถุประสงค์เพื่อสรุปสถานการณ์ปัจจุบันเกี่ยวกับปัญหาสุขภาพของผู้ป่วยสูงอายุที่เข้ารับการรักษาในไอซียูและผลลัพธ์ของการรักษาที่เกิดขึ้นในประเทศกลุ่ม LMICs

วิธีการศึกษา คณะผู้วิจัยทำการสืบค้นจาก 7 ฐานข้อมูล เพื่อค้นหาบทความวิจัยที่ศึกษาเกี่ยวกับลักษณะและการเจ็บป่วยของผู้ป่วยที่มีอายุ 60 ปีขึ้นไปที่เข้ารับการรักษาในไอซียูและผลลัพธ์ของการรักษาที่เกิดขึ้นในประเทศกลุ่ม LMICs ครอบคลุมการวิจัยโดยการสังเกตทุกรูปแบบที่ตีพิมพ์ระหว่าง พ.ศ. 2553-2562 โดยใช้เกณฑ์การประเมินคุณภาพในการทบทวนวรรณกรรมอย่างเป็นระบบและการวิเคราะห์อภิมานตามข้อกำหนดของ PRISMA และแบบตรวจสอบรายการของ Joanna Briggs Institute (JBI)

ผลการศึกษา บทความวิจัยจำนวน 10 บทความ จาก 1,486 บทความจากทุกแหล่งที่เข้าเกณฑ์การคัดเข้า ครอบคลุมผู้สูงอายุ 4,915 คน ที่เข้ารับการรักษาในไอซียูทั่วไป 6 แห่ง และเฉพาะทาง 13 แห่งจาก 7 ประเทศในกลุ่ม LMICs คุณภาพของบทความที่ได้ทบทวนโดยรวมอยู่ในเกณฑ์ปานกลาง ผลการวิจัยพบว่าอัตราตายของผู้ป่วยหนักสูงอายุในหอผู้ป่วยวิกฤตและในโรงพยาบาลรวมเฉลี่ยอยู่ที่ 15.6% (95% CI = 14.1-17.2, p = 0.04, I^2 = 96.9%) และ 33.3% (95% CI = 22.5-43.9, p<0.001, I^2 = 46.6%) มีระยะเวลาครองเตียง (LOS) ในไอซียูและในโรงพยาบาลเฉลี่ย (S.D.) = 6.7 (10.6) และ18.8 (8.6) วัน โดยมากกว่าหนึ่งในสี่ของผู้ป่วยมีอาการรุนแรงและช่วยเหลือตนเองไม่ได้ตั้งแต่แรกรับ การติดเชื้อและปัญหาที่เกี่ยวข้องมักพบในระหว่างที่ผู้ป่วยรับการรักษาอยู่ในไอซียู

สรุปผลการศึกษา ผู้ป่วยหนักสูงอายุในประเทศกลุ่ม LMICs มักมีอาการรุนแรงตั้งแต่แรกรับและมีอัตราตายในหออภิบาลผู้ป่วยวิกฤติมากกว่าร้อยละสิบ ผู้ป่วยที่มีภาวะไตวายเฉียบพลัน มีภาวะสับสน ขาดสารอาหาร มีโรคร่วมและ/หรือติดเชื้อในกระแสโลหิตเป็นปัจจัยเสี่ยงของการตายและผลลัพธ์การรักษาที่ไม่พึงประสงค์อย่างมีนัยสำคัญ

คำสำคัญ ผู้ป่วยสูงอายุ ปัญหาสุขภาพ ผลลัพธ์การรักษา หออภิบาลผู้ป่วยวิกฤต ประเทศที่มีรายได้น้อยและรายได้ปานกลาง

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Health problems and health care outcomes of older patients admitted to intensive care unitsin the low- and middle-income countries: A systematic review and meta-analysis

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Abstract

Introduction Older patients admitted to intensive care units (ICUs) hada high mortality rate, particularly in the low- and middle-income countries (LMICs).

Objectives This systematic review and meta-analysis aims to summarize current prevalence of health problems and health care outcomes of older patients admitted to ICUs in the LMICs.

Methods We searched seven databases to identify original studies investigating profiles of ICU admissions of patients aged 60 or overand health care outcomes in the LMICs.All types of observational studies published from 2010 to 2019 were eligible. Quality assessment of articles used the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) and the Joanna Briggs Institute Checklists (JBI).

Results Tenout of 1,486 observational studies from all sources enrolling a total of 4,915 critically ill older patients from six general- and thirteen specialty ICUs in seven LMICs were included. The overall quality of the studies was moderate. ICU- and in-hospital mortality pooled rates of the older patients were 15.6% (95% CI = 14.1-17.2, p = 0.04, I^2= 96.9%) and 33.3% (95% CI = 22.5-43.9, p<0.001, I^2 = 46.6%). Their pooled means (S.D.) of ICU and in-hospital length of stay were 6.7 (10.6) and 18.8 (8.6) days. Over one-fourth of them had severe conditions and loss of functional independence on ICU admission. Infection-related problems were evidenced during ICU stays.

Conclusion Critically ill older patients in the LMICs largely have severe conditions on ICU admission with over one-tenth of ICU mortality. Patients with acute kidney injury, delirium, malnutrition, comorbid illnesses, and/or sepsis significantly have increased risk of death and adverse outcomes.

Keywords Older patients, Health problems and outcomes, Intensive care unit, Low - and middle-income countries

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Introduction

Population ageing is a worldwide phenomenon, particularly in the low- and middle-income countries (LMICs).The United Nations recently reported that this population group had dramatically increased to 962.3 million in 2017 and two-thirds of them were residing in Asia-Pacific region (549.2 million (57.1%), Africa (68.7 million (7.1%), and Oceania (6.9 million (0.7%)[2]. High vulnerability to chronic and degenerative diseases, coupled with problems such as comorbidities, frailty, and disability have inevitably led the older population to manifest with complex health burdens thereby increasing needs for admission to hospitals with specialized and intensive care facilities[3]. Besides physiologic changes accompanying ageing processes, the increased burdens of critical illnesses among older populationin countries with limited resources are more likely to be associated with growing urbanization, emerging epidemic diseases, and access to health care systems[4].In the literature, older adults had higher proportion of ICUs admissionin both LMICs and high-income countries[4,5]" However, the mortality rate was notably higher among those in the LMICs[6]. Current available literature addressed that the severity of illness coupled with pre-existing comorbidities among older population were significant contributing factors to ICU outcomes[7]. Determinants of illness severity, prognosis, and clinical outcomes, explicitly patterning among the older population admitted to ICUs, are, therefore, in need of further investigation[6,8].

ICU has long been a life saving unit for patients at time of life-threatening period with a wide range of acute and critical health problems. However, ICU care is one of the most demanding types of service, especially for resource and specialty staff, in health care system. Besides, beneficial of ICU admission among older patients in the LMICs is still a critical debatable issue[9,10]

This systematic review and meta-analysis study sought to provide valuable insight into characteristics of intensive care for older patients, the prevalence of critical illnesses or health problems, received treatments, length of stay, and mortality rate both in ICU and in-hospital patterning in the LMICs. This database will inform the health personnel, hospital administrators and policymakers to consider effective solutions for decreasing burdens among older population before the manifestation of and during critical illness in health care services.

Methods

This systematic review was conducted and reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines[12]. Eligible studies included all types of observational studies, ranging from cross-sectional, retrospective or case-controlled, to prospectiveor cohort studies that reported on people aged 60 years or over admitted to ICU and health service

outcomes. This study mainly focused on ICU older patients in the setting of the Low- and Middle-Income Countries (LMICs)[13]. Studies published from June 1, 2010, through May 31, 2019, and written in the English language were considered for inclusion in this review. We excluded the studies such as narrative reviews, editorials, case reports, and case-series, as well as observational studies focusing on multiple age groups that did not show the study outcomes of the older subgroup.

Search strategy

We electronically searched seven databases: PUBMED, EBSCO, CINAHL, Science Direct, Web of Science, ASEAN Citation Index, and Thai-Journal Citation Index to identify original studies based on the inclusion criteria. The initial keywords included: *(older adult OR elderly person OR aged population OR senior citizen) AND (intensive care unit) AND (prevalence OR incidence OR disease OR cause of admission) AND (mortality OR survival OR length of stay) AND (Functional ability OR health OR quality of life) AND (treatment) AND (low-income countries OR middle-income countries OR low- and middle-income countries OR developing countries).* The references from selected articles and reviews were manually searched for additional studies from all sources, including grey literature sources such as the Ministry of Health and Medical Schools in Vietnam and Thailand. A protocol for this review has not been published separately.

Study selection and data extraction

Two authors independently evaluated the retrieved titles and abstracts of all articles to identify potentially relevant studies, specifically focused on the outcome reference to ICU- and or hospital mortality of the critically ill older patients in an intensive care unit of the LMICs. Although the primary outcome was health care outcome such as ICU mortality, hospital mortality was later added to the primary outcome to increase more chances of findings. We also focused on two categories of secondary outcomes, including 1)patient-centred outcomes, i.e., health problems or causes of ICU admission, severity, comorbidities, and functional abilities, as well as the quality of life; and 2)health services utilization, i.e., ICU length of stay (ICULOS), in-hospital length of stay (In-HOSLOS), receiving mechanical ventilation (MV), MV length of stay (MVLOS) and ICU treatment supports. We were able to initially identify 1,704 articles with an additional of six hand searching articles to fulfil eligibility.

The articles that met inclusion criteria after title and abstract review were subject to full-text review based on eligibility criteria. Any disagreement in this step was resolved by discussion and consensus. Both authors, DL and PH, independently extracted data from the search studies. Extracted data included: author (s), study design, ICU specialty and number of bed, number of the older patients in each study, causes of ICU admission and/or underlying diseases, and outcomes, both primary and secondary.

Assessment of quality

Our study used the Joanna Briggs Institute (JBI) critical appraisal checklists for two types of observational studies to assess for study quality, namely the JBI Critical Appraisal Checklist for Cohort Study[14] and the JBI Critical Appraisal Checklist for the Case-controlled Study[15]. Each checklist had three domains: a selection of the target group, comparability of the target groups, and outcome quality. With a total score of 0-11 points, the overall quality scores for the cohort study were divided into three levels: low (0-5 points), moderate (6-8 points), and high (9-11 points). Based on a total score of 0-10 points, the overall quality scores for the case-controlled study were divided into three levels: low (0-4 points), moderate (5-7 points), and high (8-10 points). (Appendix 2).

Data analysis

Data were presented using descriptive statistics such as frequency and percentage for categorical variables, as well as mean and standard deviation (S.D.) or median and interquartile range (IQR) for numerical variables depending on the distribution of the available data. To summarize an overall- and subgrouping prevalence and outcomes of the ICU older patients in different studies, we converted the median and interquartile range of some variables into mean and standard deviation to further calculate for pooled means and pooled standard deviations where appropriate[13,16,29].

A meta-analysis was performed, where possible using the Review Manager 5.3 Software (Cochrane Collaboration)[30]. We pooled outcome data from each study, both adjusted- and unadjusted data. We also calculated the pooled risk ratio (RR) and 95% confidence intervals (95%CI) using a random-effects model for dichotomous outcomes and weighted mean difference with 95% CIs for continuous data. The pooled prevalence of in-hospital and ICU mortality, receiving MV and other treatment modalities, having infection related problems and complications were analyzed using the Microsoft Excel Program[29]. Subgroup analyses for the association of nutritional status, some health problems, and ICU mortality of this population group were also performed. Statistical heterogeneity was determined using the Mantel–Haenszel (M–H) Chi-squared test and the interclass correlation (I^2) statistic[30]. Significant heterogeneity was defined as $I^2 > 50\%$ or as $p < 0.05$ with the Chi-square test. We considered an unadjusted, two-sided $p < 0.05$ to be statistically significant. Funnel plots were used for publication bias (Appendix 4).

Results

The initial search of seven databases and hand searching identified 1,704 articles and abstracts. After screening the titles and abstracts, 138 duplicates and 1,480 unrelated papers were excluded. Ninety-two full-text articles from databases (n = 92) and further hand-searching articles based on the cited

references in the previously reviewed full-text articles (n = 6) were additionally assessed; 82 studies did not meet the inclusion criteria, leaving a total of ten studies fulfilling eligibility for final analysis (Appendix 1).

General characteristics of the studies

The characteristics of the included studies are summarized in Tables 1 and 2. Out of ten included studies, four were retrospective[17,18,20,21] and six were prospective studies[19,22–26]. Based on overall listed affiliations, nine studies had been carried out in the middle-income countries[18-26,] and only one study had been carried out in the lower-income country[17]. The time duration of data collection in these studies was in an average (S.D.) of 3.0 (2.8) years, and a range of 0.5- 8.5 years. The included studies collectively described 19 individual ICUs in tertiary referral hospitals of the universities or academic institutes located in 19 cities of seven LMICs. Of which, eight studies carried out in a single-center[17,19,21–25] one study carried out in two of a single-centre serving regional level[18], and one study was carried out in nine of a single-centreof the affiliated universities across one country.[26] Of these 19 ICUs, six were a general or mixed type of ICUs that admitted patients in a broad range of critical illnesses and age groups; the other 13 were specialty ICUs, including one medical, one respiratory, two neurological, and nine surgical. Based on six ICUs with data, the study ICUs had an average (S.D.) of 17 (12.4) beds and a range of 6-38 beds.

Of 4,916 older patients enrolled in the ten studies (men = 58.0%, average age (S.D.) = 74.3 (7.2) years), eight studies reported on patients aged 65 years and over (4,617, 93.9%), while the other two studies reported on patients aged 60 years and over (299, 6.1%). Based on six ICUs in five studies[18–21,23], critically ill older adults admitted to general or mixed ICUs constituted 45.4% (1,820 out of 4,010) of a total number of patients at all ages. Additionally, five studies made comparisons.

Table 1 Characteristics of the included studies and samples

Reference	Study design (Data year)	Inclusion criteria	Exclusion criteria	Sample Characteristics		Severity scores Comorbidities Mean (S.D.) or Median(IQR) or n (%) {Nutrition state n (%)}	Admission morbidity and outcome assessed	Outcome report by age group (Y/N)
				Number (%) [Male n (%)]	Mean age in year (S.D.) or Median (IQR)			
Giannasi (2017)[22]	Prospective observational single-centre study in a mixed ICU in Argentina (2011-2012)	Aged ≥65 years with mechanical ventilation ≥48h	Chronic degenerative diseases	249 [133 (53.0)]	77(70;84) years	APACHE II: 20(7) Charlson index 6.0(4.0, 8.0) {SGA-A 97(44); SGA-B 73(33); SGA-C 51(23)}	Morbidity, in-hospital and ICU mortality prognostic factors, health service utilization, ADL, QoL	Yes
Jayalakshmi (2014)[18]	Retrospective observational double-centre study in 2 Neurological ICUs in India (2005-2013)	All patients with convulsive SE admitted to NICU	Complex partial SE, absence SE, simple partial SE, myoclonic SE, psychogenic SE, and non-convulsive SE	Subgroup of 23 convulsive SE patients >65 years [15(65.2)]	NA	NA	Morbidity,in-hospital and ICU mortality prognostic factors,	Yes
Lankoandé (2018)[17]	Retrospective observational single-centre study in a mixed ICU in Burkina Faso (2011-2015)	Aged ≥65 years	NA	237 [167(70.5)]	71.7(6.1) years	GCS 9.6(4.0) Charlson index 4.8 (>4-89.4%) Comorbidity 191(80.6)	Morbidity, in-hospital and ICU mortality prognostic factors, health service utilization	Yes

Table 1 Characteristics of the included studies and samples (Ext.)

Reference	Study design (Data year)	Inclusion criteria	Exclusion criteria	Sample Characteristics		Severity scores Comorbidities Mean (S.D.) or Median(IQR) or n (%) {Nutrition state n (%)}	Admission morbidity and outcome assessed	Outcome report by age group (Y/N)
				Number (%) [Male n (%)]	Mean age in year (S.D.) or Median (IQR)			
Limpawattana (2016)[25]	Prospective observational single-centre study in a medical ICU in Thailand (2013-2014)	Aged ≥65 years	Previously stayed in ICU, comatose, severe aphasia, or having a severe hearing impairment	99 [46 (46.5)] Delirium 44(44.4)	76.4(7.3) years	APACHE II: All 16.7(4.9), Delirium 23.8(0.9), Non-delirium 19.0(0.7)	Morbidity, pre-existing problems, health service utilization, ADL	Yes
Poluyi (2016)[21]	Cross-sectional research study single-centre study in a mixed ICU in Nigeria (2010-2015)	All patients	NA	A subgroup of 99 patients >60 years [54(54.5)]	70.6(8.3) years	NA	Morbidity, ICU mortality	Yes
Sharma (2012)[19]	Prospective observational single-centre study in a Respiratory ICU in India (2008-2009)	Aged ≥18 years	Deaf or unable to speak or understand Hindi, English or Punjabi, whose caregivers refused consent	A subgroup of 24 patients ≥65 years with delirium 23(95.5)	66.9(1.8) years	APACHE II 19.5(5.6)	Morbidity, and ICU mortality	Yes

Table 1 Characteristics of the included studies and samples (Ext.)

Reference	Study design (Data year)	Inclusion criteria	Exclusion criteria	Sample Characteristics		Severity scores Comorbidities Mean (S.D.) or Median(IQR) or n (%) {Nutrition state n (%)}	Admission morbidity and outcome assessed	Outcome report by age group (Y/N)
				Number (%) [Male n (%)]	Mean age in year (S.D.) or Median (IQR)			
Shpata (2015)[23]	Prospective observational single-centre study in a mixed ICU in Albania (2008-2009)	Aged ≥18 years	stayed <72 hours or stayed in the ICUs for temporary monitoring	A subgroup of 459 patients ≥65 years [270 (58.8)]	74.41(5.93) years	APACHE II 19.0(5.6) Malnutrition risk 327(71.2)	Morbidity, pre-existing problems in-hospital and ICU mortality, prognostic factors, health service utilization	Yes
Sodhi (2014)[20]	Retrospective observational single-centre study in a mixed ICU in India (2011-2012)	All patients newly admitted to ICU	Incomplete records and/ or previously stayed in ICU	A subgroup of 1,216 patients ≥65 years [738(60.7)]	73.8(7.15) years	APACHE II 18.2(8.5)	Morbidity, ICU mortality, health service utilization	Yes
Trongtrakul (2016)[26]	Prospective observational multicenter study in 9 surgical ICUs in Thailand (2011-2013)	Aged ≥65 years	NA	2,310 [1,329 (57.3)] AKI 445 (19.3) [289(64.9)]	75.8(7) years	APACHE II: All 12.0 (8.0-16.0) AKI 16.0 (12.0-22.0), Non-AKI 11.0(8.0-15.0)	Morbidity, pre-existing problems, in-hospital and ICU mortality, prognostic factors, health service utilization	Yes

Table 1 Characteristics of the included studies and samples (Ext.)

Reference	Study design (Data year)	Inclusion criteria	Exclusion criteria	Sample Characteristics		Severity scores Comorbidities Mean (S.D.) or Median(IQR) or n (%) {Nutrition state n (%)}	Admission morbidity and outcome assessed	Outcome report by age group (Y/N)
				Number (%) [Male n (%)]	Mean age in year (S.D.) or Median (IQR)			
Yokota (2017)[24]	Prospective observational single-centre study in mixed ICUs in Brazil (2014-2015)	Aged ≥60 years	Chronic kidney disease stage 4, 5; Kidney transplantation, ICU stay <24 h, and having been already ICU admitted AKI patients	200 [107(53.5)] AKI 54(27.0) [28(51.8)]	70.94(7.8) years	APACHE II: All 12.7(5.9) AKI 17.5(7.5), Non-AKI 11.3(4.2)	Morbidity, pre-existing problems,in-hospital and ICU mortality, prognostic factors, health service utilization	Yes

Abbreviation: ICU-intensive care unit, AKI-acute kidney injury, QoL-quality of life, APACHE IIscore-acute physiology and chronic health evaluation score, ADL-Activities of Daily Living index, GCS-Glasgow coma score, S.D.-standard deviation, IQR-interquartile range, SE-status epilepticus

Table 2 Outcomes of the older adult patients during ICU stay and mortality rates

Study	Mortality Rate (MR)		Length of Stay (LOS)		Mechanical Ventilation (MV)		Others n (%)
	In-hospital MR n(%)	ICU MR n(%)	In-hospital LOS (days) Mean (S.D.) or Median (IQR)	ICU LOS (days) Mean (S.D.) or Median (IQR)	Receiving MV n(%)	MV LOS (days) Mean (S.D.) or Median (IQR)	
Giannasi (2017)[22]	130(52.2)	109(44.0)	Total 26 (N = 249); (15;48) Alive at discharge (n = 119); 37(22;64) Died during admission (n = 130); 19(11;33)**	16(9;29) 18 (11; 36) 14(8;22)**	249(100.0)	10(5;21) 9(4;27) 11(6;19)	RRT 52(20.8) Septic shock 18(7.0) RRT 12(10.0) Septic shock 6(5.0) RRT 40(31.0) ** Septic shock 12(9.0)
Jayalakshmi (2014)[18]	5(21.7)	NA	9.9(7.7)	6.7(7.4)	NA	3.9(7.0)	MV complication 3(13.0)
Lankoandé (2018)[17]	NA	173 (73.0)	NA	Total (N = 237) 5.3 (6.8) Survivors (n = 64) 5.5(5.1) Non-survivors (n = 173) 5.2(8.0)	Total 2(0.8) Survivors 0 Non-survivors 2(100)	NA	Complication in ICU: Total 89(37.5) Survivors 9(10.1) Non-survivors 80(89.9)
Limpawattana (2016)[25]	NA	NA	NA	NA	Total (N = 99); 48(48.5) Delirium (n = 44); 30(68.2) Non-delirium (n =55); 18(32.7)**		Infection: Delirium: 41(93.2) Non-delirium 44(80.0)
Poluyi (2016)[21]	NA	44(44.4)	NA	NA	NA	NA	NA
Sharma (2012)[19]	NA	5(21.7)	NA	NA	NA	NA	NA

Table 2 Outcomes of the older adult patients during ICU stay and mortality rates (Ext.)

Study	Mortality Rate (MR)		Length of Stay (LOS)		Mechanical Ventilation (MV)		Others n (%)
	In-hospital MR n(%)	ICU MR n(%)	In-hospital LOS (days) Mean (S.D.) or Median (IQR)	ICU LOS (days) Mean (S.D.) or Median (IQR)	Receiving MV n(%)	MV LOS (days) Mean (S.D.) or Median (IQR)	
Shpata (2015)[23]	NA	196(42.7)	NA	10.5(9.6)	NA	2.5(4.6)	Complications 263 (57.2) Infection 169 (36.8)
Sodhi (2014)[20]	NA	244(20.1)	NA	11.4(17.4)	354(29.1)	NA	Hemodialysis 111(9.1)
	Total 28-day-in-hospital MR (N=2,310); 335(14.5)	Total 222(9.6)	Total 15(9;26)	Total 2(1;4)	Total 1,345(58.2)	Total 2(1;5)	Sepsis: Total 475(20.6)
Tronatrakul (2016)[26]	AKI (n=445); 159(35.7) Non-AKI (n=1,865); 176(9.4)**	AKI 125(28.1) Non-AKI 97(5.2)**	AKI 17(10;29) Non-AKI 15(9;12)**	AKI 5(2;13) Non-AKI 1(1;3)*	AKI 383(86.1) Non-AKI 962(51.6)**	AKI 5(2;3) Non-AKI 2(1;4)**	AKI 232(52.1) Non-AKI 243(13.0)
Yokota (2017)[24]	NA	Total (N = 200) 49(24.5) AKI (n= 54) 26(48.1) Non-AKI (n= 146) 23(15.7)**-	NA	Total 6.9(7.9) AKI 11.4(5.4) Non-AKI 5.2(2.1)**	Total 66(33) AKI 20(37.0) Non-AKI 46(31.5)	NA	Survivors (n = 145): -Sepsis 39(26.9); -APACHE II 11.0(4.2) Non-survivors (n = 49): -Sepsis 30(61.2) -APACHE II 19.1(6.6)

Abbreviation: ICU-intensive care unit, AKI-acute kidney injury, S.D.-standard deviation, IQR-interquartile range, SE-status epilepticus, *p-value <0.05, **p-value <0.001

between specific subgroups, including patients with or without such conditions as refractory status epilepticus[18]data of patients with convulsive SE admitted in neurointensive care unit (NICU, delirium[19,25], and acute kidney injury (AKI)[24,26].

Health conditions and prevalence of health problems at ICU admission

All ten studies reported on baseline health conditions and prevalence of illnesses of older patients on ICU admission. Data could be abstracted for severity based on the APACHE II score in seven studies and Glasgow Coma Score (GCS) in one study. Pooled unadjusted data, mean (S.D.) of their APACHE II score was 15.0(6.2) with a mean range of 12.0-20.0, and available data showed illness severity was higher among the older patients with delirium (23.8(0.8))[25] comparative to the non-delirious peers (19.0 (0.7)), and among patients with AKI (16.7(7.4))[26] comparative to the non-AKI peers (11.3 (5.2)). The reported mean (S.D.) of the Glasgow Coma Score (GCS) of the older patients in one study[17] was 9.6 (4.0) with 42.1% of them (100 out of 237) being comatose (GSC < 8). For the quality of life, one study reported on the median (IQR) of the Euro Quality of Life (EQ5D), comprising 5 dimensions expressed in the time trade-off (TTO) score, of 0.7 (0.6; 1), where 1 is the maximum quality of life and 0 being correspondent to imminent death.

Comorbidity burdens, as reported by two studies[17,22], were high among older patients (n = 486) given the pooled mean (S.D.) of their Charlson Comorbidity Index was 5.4 (2.1), where the hazard ratio for score > 4 representing higher comorbidity. Two studies reflected functional independence of the patients assessed by the Activities of Daily Living Index-ADL (0 to 6) or The Barthel-ADL (0 to 100), from minimum to maximum independence. While one study[22] indicated one-fourth of the patients already had a loss of their functional independence (ADL <6 points), another study[25] (mean Barthel-ADL (S.D.)) reported that delirious patients (5.6(6.5)) were more likely to be not independent comparative to the non-delirious peers (11.1(9.0)). For nutritional status, our findings based on two studies[22,23]indicated the pooled rate of 60.6% (95%CI= 39.6-81.6, $p< 0.001$, $I^2 = 92.0\%$) of the ICU older patients were malnourished. Additionally, one study[23] reported 11.1% of ICU older patients were at a severe level of malnutrition (SGA-C) upon admission.

Nine studies reported on health problems of the ICU patients (n = 3,700) based on causes of admission or underlying problems primarily be diagnosed. Of which, top five leading health problems included 1) gastroenterological related conditions (973, 33.1%), such as non-surgical abdominal problems and peritonitis; 2) cardiovascular diseases (757, 25.7%), such as shock, stroke, heart failure, and vascular-related factors; 3) malignancy and cancer (397, 13.5%); 4) neurological related conditions (381, 13.0%), such as alteration of consciousness, cognitive problems, delirium, status epilepticus; and

5) problems requiring emergency admissions (352, 12.0%), such as poly traumatism, severe brain trauma, thermal burns, and acute metabolic complications from DM and other related metabolic factors.Besides, renal problems and AKI (296, 10.1%); respiratory problems, i.e., respiratory distress syndrome (RDS) (285, 9.7%), infection and sepsis (217, 7.4%) were also prevalent among older patients on ICU admission in this reviewstudy.

Four studies (n = 3,068) reported on pre-existing conditionsof the ICU older patients before admission, and some of them had multiple conditions[23–26].The pooled rateof hypertensionranked the highest, 64.6% (95% CI = 58.9-70.3, p < 0.001, I^2 = 0%)[24,26], while DM with the rate of 32.3% (95% CI =26.6-38.0, p < 0.001, I^2 = 85.0%), CVD with the rate of 32.0% (95% CI =29.9-34.0, p < 0.001, I^2 = 0%) and previous stroke with the rate of 13.3% (95% CI =3.7-22.8, p< 0.01, I^2 = 80.0%)[25,26] were frequently evidenced. Other pre-existing conditions such as malignancy, RDS, chronic kidney disease (CKD)[26], along with depression, cognitive impairment as well as alcohol and drug-related abused[25]were also reported.

Mortality

Nine studies reported on mortality. Data could be abstracted for in-hospital mortality in three studies, and for ICU mortality in eight studies.Pooled prevalence of in-hospital mortality rateamong the ICU older patients was 15.6% (95% CI =14.1-17.2, p= 0.04, I^2= 96.9%) (Figure 1).The pooled prevalence of ICU mortalityrevealed the rate of 33.3% (95% CI = 23.0-44.0, p<0.00001, I^2 = 98.0%) (Figure2).

Subgroup analysis revealed that ICU mortalitywas statisticallysignificantly higher for AKIolder patients comparative to their non-AKI peers (RR = 4.2, 95% CI = 2.4-7.3, p<0.00001, I^2= 78.0%)[26] (Figure3). ICU mortality of the malnourishedpatients was also higher than that of theirnormally nourished peers (RR = 1.7, 95% CI = 1.3-2.1, p<0.00001, I^2 = 16.0%)[24] (Figure4).

In-hospital and ICU length of stay (LOS)

Three studies reported in-hospital LOS[18,22,26] and seven studies reported ICU LOS[17,18,20,22–24,26]. The pooled mean of in-hospital LOS(S.D.)among the older patients admitted to ICU was 18.8 (8.6) days. Meanwhile, their pooled ICU LOS had an average (S.D.) of 6.7 (10.6) days.There was no difference in ICU LOS for patients who were survivors comparative to non-survivors, based on two studies[17,22], with the mean differences being 3.1 days (95% CI = -2.8-8.9, p = 0.31, I^2 = 88.0%) (Appendix Figure6). However, ICU LOS, based on two studies[24,26], demonstrated significant longer stays for AKIpatients comparedto their non-AKI peers with the mean differences being 5.4 days (95% CI = 4.3-6.6, p < 0.00001, I^2 = 50.0%) (Appendix Figure7).

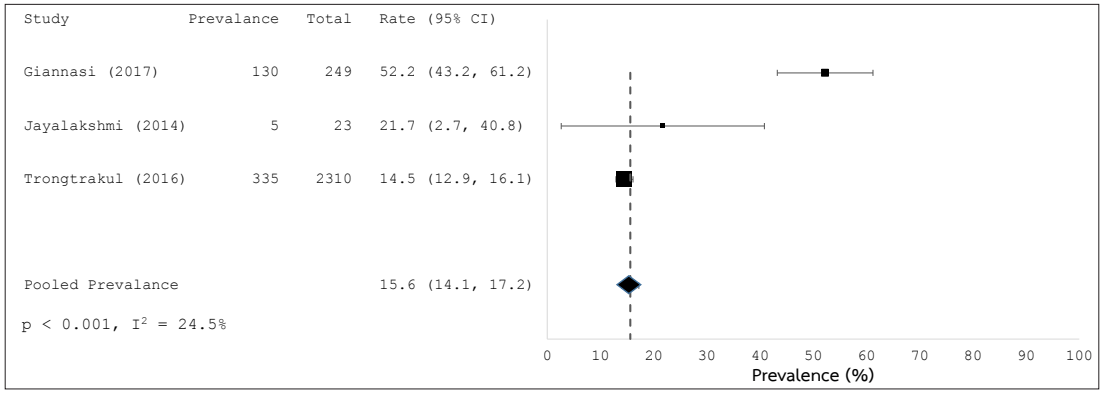

Figure 1 Prevalence of in-hospital mortality among older patients in the included studies

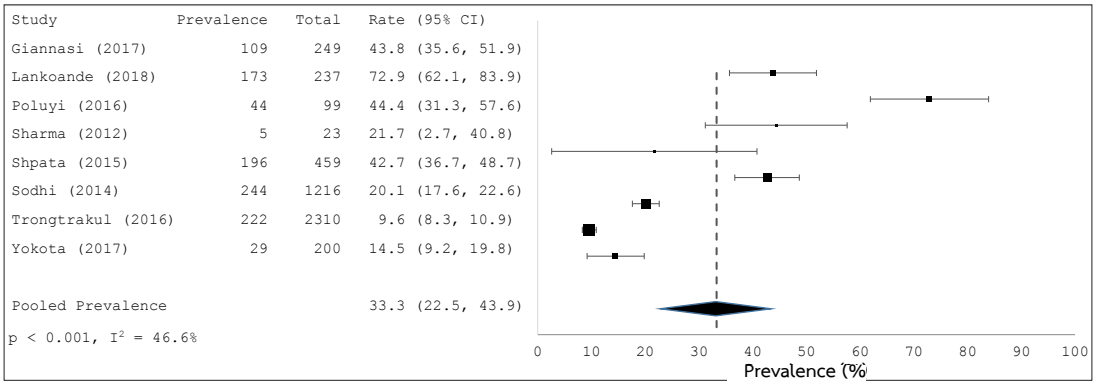

Figure 2 Prevalence of ICU mortality among older patients in the included studies

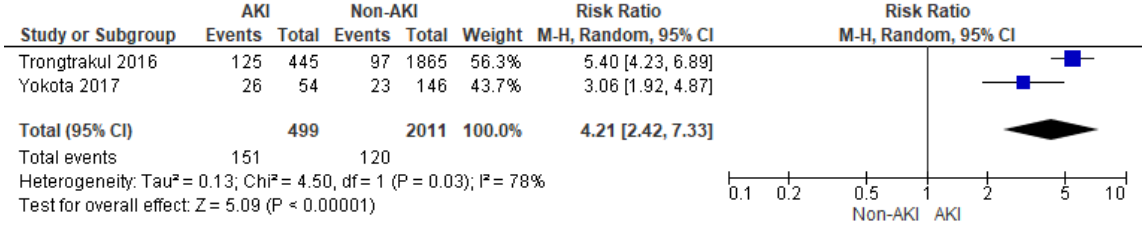

Figure 3 Risk of ICU mortality in non-acute kidney injury (Non-AKI) and AKI older patients

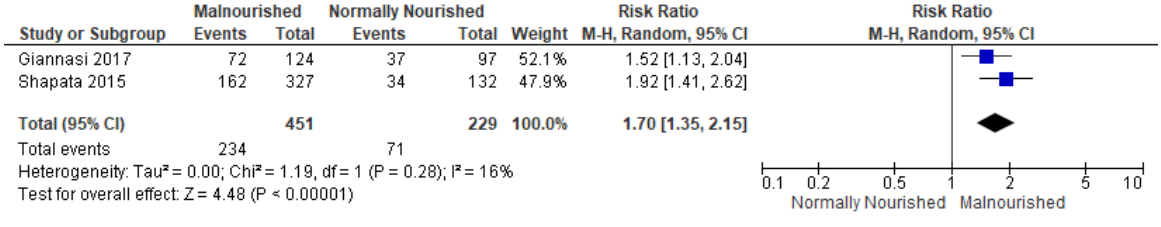

Figure 4 Risk of ICU mortality in normally nourished and malnourished older patients

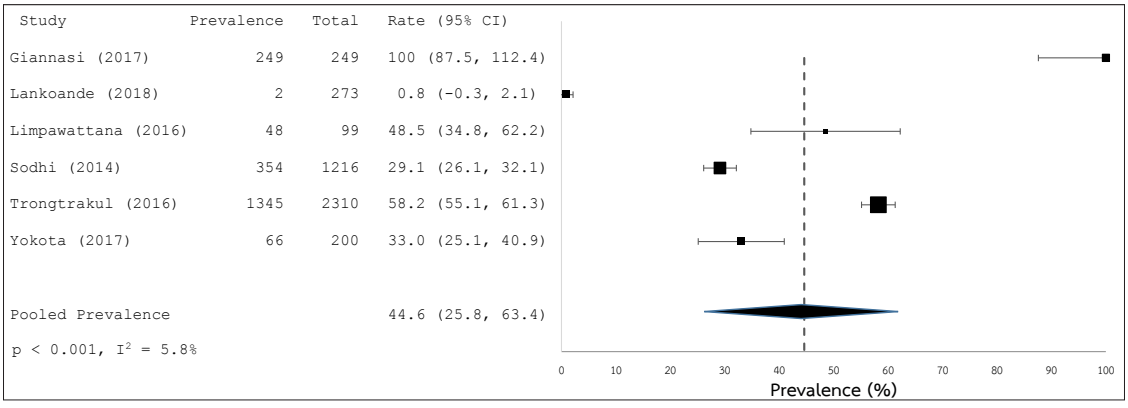

Figure 5 Prevalence of receiving mechanical ventilation (MV)

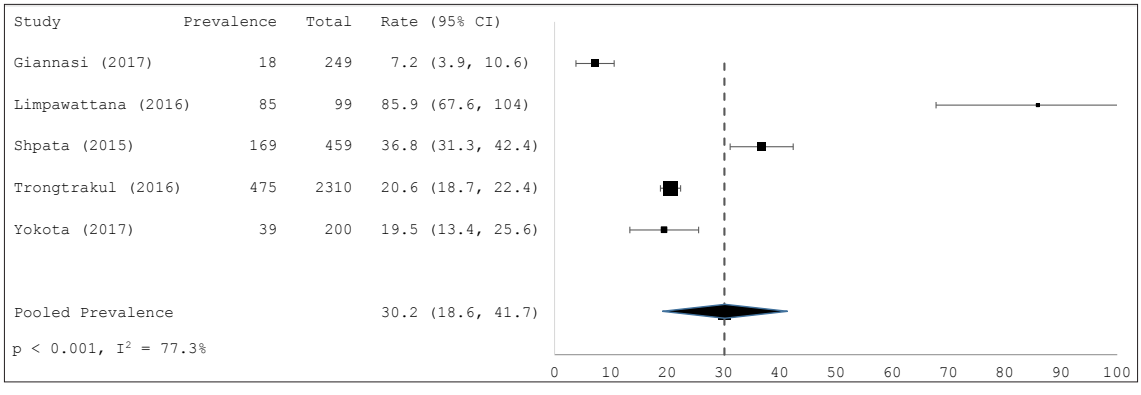

Figure 6 Prevalence of infection related problems during ICU stays

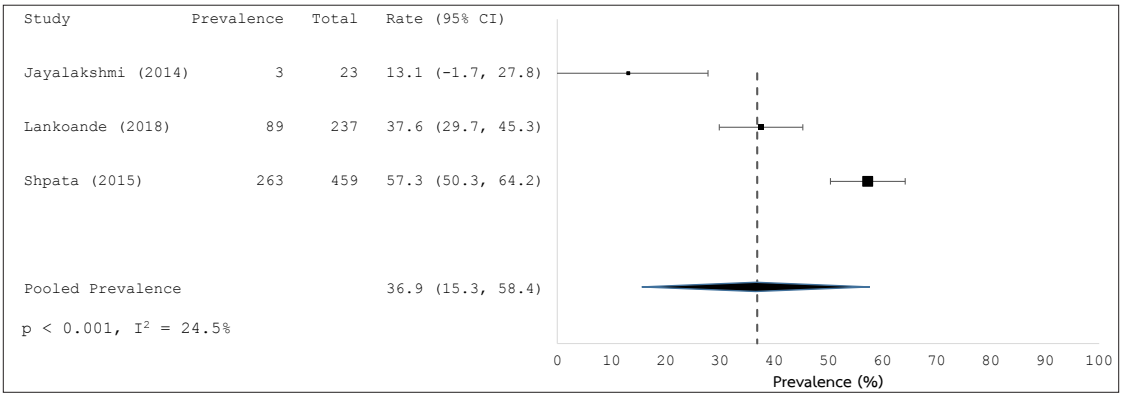

Figure 7 Prevalence of having complications during ICU stays

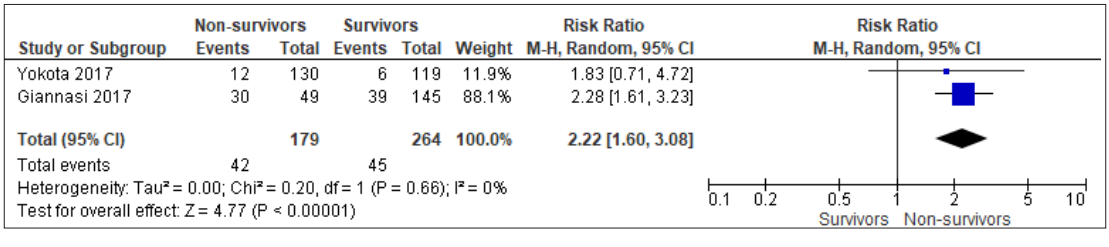

Figure 8 Risk of infection during ICU stays in older patients who were survivors and non-survivors

Mechanical ventilation (MV) and life support treatments

Six of the ten studies, which included 2,064 older ICU patients, reported on receiving MV[17,20,22,24–26]. Pooled prevalence rate of receiving MV in this population group was 44.6% (95% CI = 18.8-70.4, p = 0.0007, I^2 = 100.0%) (Figure5). Two studies[24,26] compared receiving MV between groups and found that patients with AKI significantly had received MV 2.2 times higher than their non-AKI peers (95% CI = 1.2-3.9, p = 0.01, I^2 = 85.0%) (Appendix Figure8). In addition, one study[24] reported receiving MV prevalence in delirious pateints being 4.4 times higher than their non-delirious peers (unadjusted OR = 4.4, 95% CI = 1.9-10.3, p <0.001).

Aside from receiving MV, other reported life support treatment modalities for ICU older patients in the LMICs were including renal replacement therapy (20.8%)[22], hemodyalisis (9.1%)[20], inotropic supports[20,24]and tracheostomy[20,22]. Pooled rates of receiving inotropic supports was 29.5% (95% CI = 25.3-33.7, p < 0.001, I^2 = 5.8%) and receiving tracheostomy was 18.8% (95% CI = 8.4-46.0, p = 0.17, I^2 = 98.0%), respectively (Appendix Figure9-10).

Infection related problems and having complications during ICU stays

Five out of the ten studies, which included 768 out of 3,068 older ICU patients, reported on infection related problems, either acquired infection or sepsis or septic shock during ICU stays[22–26]. Their pooled prevalence rate of infection related problems was 30.2% (95% CI=18.6-41.7, p < 0.001, I^2 = 77.3%) (Figure.6). Pooled prevalence rate of having complications during ICU stays of this group of patients, based on three studies[17,18,23], was 36.9% (95% CI = 28.2-66.9, p< 0.001, I^2 =24.5%) (Figure7).

Subgroup analysis was conducted for the comparison of having infection related problems, as well as complications during ICU stays between patients who were survivors and non-survivors. Two studies[22,24]made comparison of infection related problems between groups and found that older patients who were non-survivors significantly had 2.2 times higher risk of infection related problems than the survivors (95% CI = 1.6-3.1, p < 0.00001, I^2 = 0%) (Figure8). In line with infection related problems, older patients having complications during ICU stays in one study[17] indicated the significantly higher rate in non-survivors (89.9%) than the survivors (10.1%), p < 0.001.

Discharge description

Two studies briefly reported on the discharge of critically ill older patients[17,22]. Of which, one study, in the middle-income country, reported 47.8% of the ICU patients discharged alive from hospital[22]. Another study[17]reported on the outcomes of ICU care in the lower-income country included death in ICU (173 out of 237, 73.0%), being transferred to other wards (48 out of 237, 20.2%), hospital discharge with physician authorization (10

out of 237, 4.2%), and discharge without physician authorization (6 out of 237, 2.5%). However, both studies did not specify discharge dispositions or destinations.

Study quality

There were five high-quality studies[17,20,22,23,26] (Appendix 2). All of the ten included studies were reporting on morbidity or mortality, or both. Nine in the ten included studies reported on mortality, either in-hospital- or ICU- or both. Additionally, we also received supportive information on mortality data of the older subgroup from the corresponding author of one of the included studies[19] (Appendix 5).

Publication bias

Publication bias was assessed visually using a funnel plot for the prevalence of ICU mortality; there was no significant evidence of publication bias (Appendix 4). However, it was necessary to note that only one in the ten included studies was from the low-income country in this review study[17]. Moreover, the authors did search from grey literature sources to find unpublished research studies related to the study topics to increase more coverage of publication sources.

Discussion

This systematic review comprised of the mixture of both prospective and retrospective studies spanning 0.5-8.5 years. Most study ICUs in the LMICs were in referral hospitals of universities or academic institutes with the size of approximately 6-38 beds. Finding only one out of ten included studies from the low-income country reflects some limitations such as insufficient trained critical care staff and researchers, limited funding and infrastructure, and having barriers in compiling existing data into research and publication[4].

In this review, older population constitute nearly half of the overall critically ill patients admitted to general ICUs in the LMICs. Their average age (SD) is 74.3 (7.2) years, and over half of them are men (58.0%). Their leading health problems on ICU admission included gastroenterological related conditions (33.1%), cardiovascular diseases (25.7%), malignancy and cancer (13.5%), related neurological conditions (13.0%), problems requiring emergency management (12.0%), and other causes, namely renal problems, RDS, and sepsis. Their reported pre-existing conditions were mostly chronic degenerative diseases, such as hypertension, CVD, DM, CKD, malignancy, RDS, previous stroke, and depression, respectively from high to low.

The overall annual ICU mortality rate of 33.3% among older patients in the LMICs in this review study is higher than that of the whole critically ill patients at all ages across the globe (16.2%) reported by Vincent and colleagues in their study on global burdens of critical ill population at all ages in intensive care facilities covering 84 countries across GNI levels conducted in 2012[11]. Our findings also indicate the higher ICU mortality rates among

older patients with AKI and malnutrition. Increased mortality risks of critically ill patients in intensive care services in the lower GNI countries possibly resulted from limited trained staff and treatments or poor quality of care, as well as the type of ICU organization and management with in the country, such as a closed- and open format of ICU management, and allocation of bed-to-nurse ratio in ICU[4,11].

In-hospital mortality in our review reveals the rate of 15.6%. In-hospital mortality risk factors among critically ill patients across all ages and GNI countries reported in several studies[5,11,22,23,28] include: 1) being in countries with lower GNI; 2) being older than 75; 3) having higher severity score; 4) being admitted under the medical or traumatism ICU related services; 5) being admitted from hospital floor; 6) having comorbid cancer or chronic heart failure; 7) receiving treatments such as immune suppression, MV, or RRT; 8) being malnourished; and 9) being affected by cirrhosis.

Our review study shows average of ICU LOS and in-hospital LOS in the LMICs of 6.7 days and 18.8 days, respectively, which are longer period than the reported average of 3.7 and 11.7 days in the whole study critically ill patients at all ages, and the average of 4.3 and 8.3 days in such a group of patients in the middle-income countries reported by Vincent and colleagues[11].

For ICU life support treatments, our findings indicate mechanical ventilation, inotropic support, and tracheostomy were required by 44.6%, 29.5%, and 18.8% of the patients, respectively. Receiving MV among critically ill older patients in this review study is slightly higher than that of the critical ill patients at all ages in the lower-and lower-middle-income countries (35.5%) but lower than that of the whole critical ill patients across the globe (53.7%) and the upper-middle-income countries (55.0%) reported by Vincent and colleagues[11]. Our study finds the higher rate of receiving MV among ICU older patients with delirium and AKI approximately 2 and 4 times higher than those without such conditions, respectively.

Inotropic supports are required by over one-fourth of the ICU older patients in this review study. However, the recent meta-analysis study[32] on the effect of inotropes and vasopressors on mortality based on the 28,280 critically ill patients at all ages in intensive care facilities from 177 randomized clinical controlled trials points out that inotrope and vasopressor therapy is not associated with differences in mortality rates of the overall study population and the majority of their study sub-settings. Our reported tracheostomy in the ICU older patients (18.8%) is lower than the rate of 32.2% of the critically ill patients admitted to ICU requiring MV for at least 14 days in a tertiary care hospital in Taiwan[31]. In such a study, Lin and colleagues[31] revealed that the ICU patients receiving tracheostomy had lower in-hospital mortality and higher successful weaning rate than those receiving translaryngeal intubation.

RRT[22] and haemodialysis[20] were also served as the treatment modalities for 10.0-20.0% of the patients. Our finding from one study ICU indicates 21.0% of older patients receiving RRT[22], which is higher than the rates of 12.2% and 7.2-13.9% patterning among the whole study population of all ages across the globe and the study population in the LMICs reported by Vincent and colleagues[11].

The severity of condition (mean APACHE II score (SD)) among older patients on ICU admission in the overall LMICs in our review study is 15.0 (6.2) points, with the more severe conditions in the critically ill older patients with delirium (23.8 (0.8) points) and AKI (16.7 (7.4) points). Despite the slightly less severity of conditions on ICU admission, relative to the mean APACHE II score (SD)) of 17.9 (9.4) points of the overall study population in the Vincent and colleagues' study[11], our findings indicate nearly half of the ICU older patients (42.1%) are comatose with GSC < 8, and half of them have high comorbidity (mean Charlson Comorbidity Index (SD) = 5.4 (2.1)). Additionally, one-fourth of them already has functionally dependence (ADL <6 points).

The prevalence rate of infection related problems among older patients during ICU stays of 30.2% in our study is in line with the rate of 29.5% reported in the whole study population by Vincent and colleagues[11]. Septic shock is also reported among 7.0% of the older group of patients in one study ICU in this review study, which is comparable to the rate of 9.8% of the overall study population reported in the aforementioned study[11]. Sepsis is generally found to be associated with ICU and in-hospital mortality. In the study by Vincent and colleagues[11], ICU patients with sepsis are more likely to have 1.3 times increased risk of in-hospital mortality than those with out such a condition. The same study indicates that patients with sepsis constitute approximately over one-third of the reported in-hospital mortality rate of 22.4% in the whole study critically ill patients at all ages.

For nutritional status, our findings indicate 60.6% of the ICU older patients are malnourished with some of them being in a severe level. Malnourished critically ill older patients significantly have poor clinical outcomes such as infection, complications, elevated mortality, and ICU length of stay >14 days[23].

This current systematic review study has some limitations. First, we were able to capture data from only one study based on one ICU in the lower-income country[17], although our exhaustive search strategies, this may due in part to the lack of relevant publications in this setting. There was substantial variability in availability of relevant data among the included studies, consequently we often relied on one or two studies in explaining some health problems and health care outcomes of the patients. Additionally, many health systems have changed drastically since the publication of the included studies and given the ten-year time frame of our data collection, some described features of critical care may be outdated.

Conclusion

Critically ill older patients are population group that utilize nearly half of the intensive care services in the LMICs.Over one-fourth of them already have severe conditions on ICU admission. Gastroenterological related conditions, cardiovascular diseases, malignancy and cancer, neurological related conditions, and problems requiring emergency admission, such as polytraumatism, severe brain trauma, thermal burns, and acute metabolic complications were leading causes of ICU admission of the older population in the LMICs. In this study, we demonstrate significantly increased risk of mortality and adverse outcomes in critically ill older patients with acute kidney injury, delirium, malnutrition, comorbid illnesses, and infection related problems, particularly sepsis. Having severe conditions on admission and higher ICU mortality rate among critically ill older patients serve as the most important burdens of intensive care in the LMICs that need efforts to strengthen investigation and implementation of effective care plans and management solutions for the critically ill older group in intensive care- and hospital service.Such burdens also raise the needs for effective preventive strategies in a policy level to improve health and quality of life of the increasing older adult population in the LMICs.

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