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REVIEW ARTICLE

RISK MANAGEMENT IN INTENSIVE CARE UNITS WITH ARTIFICIAL INTELLIGENCE TECHNOLOGIES: SYSTEMATIC REVIEW OF PREDICTION MODELS USING ELECTRONIC HEALTH RECORDS

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ABSTRACT

Clinical risk assessments should be made to protect patients from negative outcomes, and the definition, frequency and severity of the risk should be determined. The information contained in the electronic health records (EHRs) can use in different areas such as risk prediction, estimation of treatment effect ect. Many prediction models using artificial intelligence (AI) technologies that can be used in risk assessment have been developed. The aim of this study is to bring together the researches on prediction models developed with AI technologies using the EHRs of patients hospitalized in the intensive care unit (ICU) and to evaluate them in terms of risk management in healthcare. The study restricted the search to the Web of Science, Pubmed, Science Direct, and Medline databases to retrieve research articles published in English in 2010 and after. Studies with a prediction model using data obtained from EHRs in the ICU are included. The study focused solely on research conducted in ICU to predict a health condition that poses a significant risk to patient safety using artificial intellegence (AI) technologies. Recognized prediction subcategories were mortality (n=6), sepsis (n=4), pressure ulcer (n=4), acute kidney injury (n=3), and other areas (n=10). It has been found that EHR-based prediction models are good risk management and decision support tools and adoption of such models in ICUs may reduce the prevalence of adverse conditions. The article results remarks that developed models was found to have higher performance and better selectivity than previously developed risk models, so they are better at predicting risks and serious adverse events in ICU. It is recommended to use AI based prediction models developed using EHRs in risk management studies. Future work is still needed to researches to predict different health conditions risks.

Keywords: risk management, artificial intelligence, electronic health record, intensive care unit

INTRODUCTION

Although the low performance or lack of health services, 4-17% of the patients experience poor health outcomes up to mortality. Poor health outcomes and adverse situations arising from health services put a heavy economic burden on countries (1). A working framework should be drawn in which poor health outcomes are prevented, patient safety is ensured, qualified, safe and effective service is provided and information technologies are at the focus (2,3). Risk management carried out in order to ensure patient safety, increases the quality of care and reduces the costs of risks is one of the requirements of quality studies in healthcare institutions (4,5). Risk management in healthcare includes recognizing the synergistic effect of risks at every stage of the service, reducing uncertainties and variability, and increasing patient safety and clinical and administrative activities carried out in order to protect the existence of the institution (5,6). According to International Organization for Standardization (ISO) 31000: 2009 Risk Management Standard, risk management is an integral part of organizational processes (7). The scope of risk management is defined as patient, employee, facility, environmental safety and administrative financial processes in the "Accreditation Standards for Healthcare (SAS)" of the Ministry of Health of the Republic of Türkiye. Within the scope of determining and analysing the risks, " Clinical risk evaluations must be conducted for protecting patients against adverse results (allergy, pressure ulcer, fall risks, risks arising from devices etc.) " and "analysing and evaluating the risks for patient safety, determining the risk level and making the necessary improvement studies according to the analysis results" are requirements (8). The clinical risk assessment process includes defining the risk, determining its frequency and severity, eliminating the risk and conducting cost-effectiveness studies according to the realization of the risk (9).

Early prediction of disease progression is an ongoing challenge in healthcare. Accurate prediction of the poor outcomes that may develop in patients can provide early intervention and risk anticipation provides healthcare workers with an opportunity to reduce preventable adverse events (10-12). In health services, there are risk scoring methods used to predict risk. Frequently Braden, Acute Physiology and Chronic Health Evaluation (APACHE), Simplified Acute Physiology Score (SAPS), Glascow Coma Score (GCS), Sepsis-related Organ Failure Assessment (SOFA), Organ Dysfunction Score (MODS), Predisposition, Infection, Response Scoring systems such as organ dysfunction (PIRO), Mortality in Emergency Department Scores (MEDS) are used (12,13). After Industry 4.0, machine learning (ML), artificial intelligence (AI) technologies are used in healthcare services to provide quality healthcare to patients by saving workload, to reduce human-induced errors in diagnosis and treatment processes, and to support medical decision processes. The areas where AI technologies are most frequently used in healthcare are diagnosis, determination of post-illness complications and medical prediction (14-16).

ICUs; are one of the most suitable areas for predictive research in the hospital, as detailed clinical data on a daily basis to closely monitor patients are collected and involve high-risk decision-making processes. (17,18).

The application of prediction models developed to improve the quality of clinical care has become possible with the increase in the volume, detail and availability of EHR in the last decade. The information contained in the EHRs provides the opportunity to conduct research in different areas such as risk prediction, patient subtyping, estimation of treatment effect and patient similarity analysis. Risk prediction derived from EHR can be calculated and updated automatically during the inpatient time (19,20).

The aim of this study is to bring together the researches on prediction models developed with artificial intelligence technologies using the EHRs of patients hospitalized in the ICU by a systematic review method and to evaluate them in terms of risk management in healthcare. With the information obtained, it is aimed to create a resource for health professionals.

MATERIAL AND METHODS

The research design was made in accordance with the "Checklist for preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement" (21).

The literature review for the study was conducted in Pubmed, Science Direct, Medline, and Web of Science databases. Keywords "electronic data and intensive care unit, electronic health data and intensive care unit, electronic health record and intensive care unit, medical informatics and intensive care unit" are used. This study is limited to research articles whose full text can be accessed in databases specified between December 1-31; 2020.

The studies in the specified databases were combined by using the EndNote X9.2 program and duplicate studies were removed through this program. The quality evaluation criteria developed by Kmet et al. (2004) were used in the quality evaluation of the articles. The selection of the studies was made according to the inclusion and exclusion criteria determined by the researchers.

Inclusion Criteria

Studies with a prediction model using data obtained from EHRs in the ICU are included. Research articles published in English in 2010 and after were included

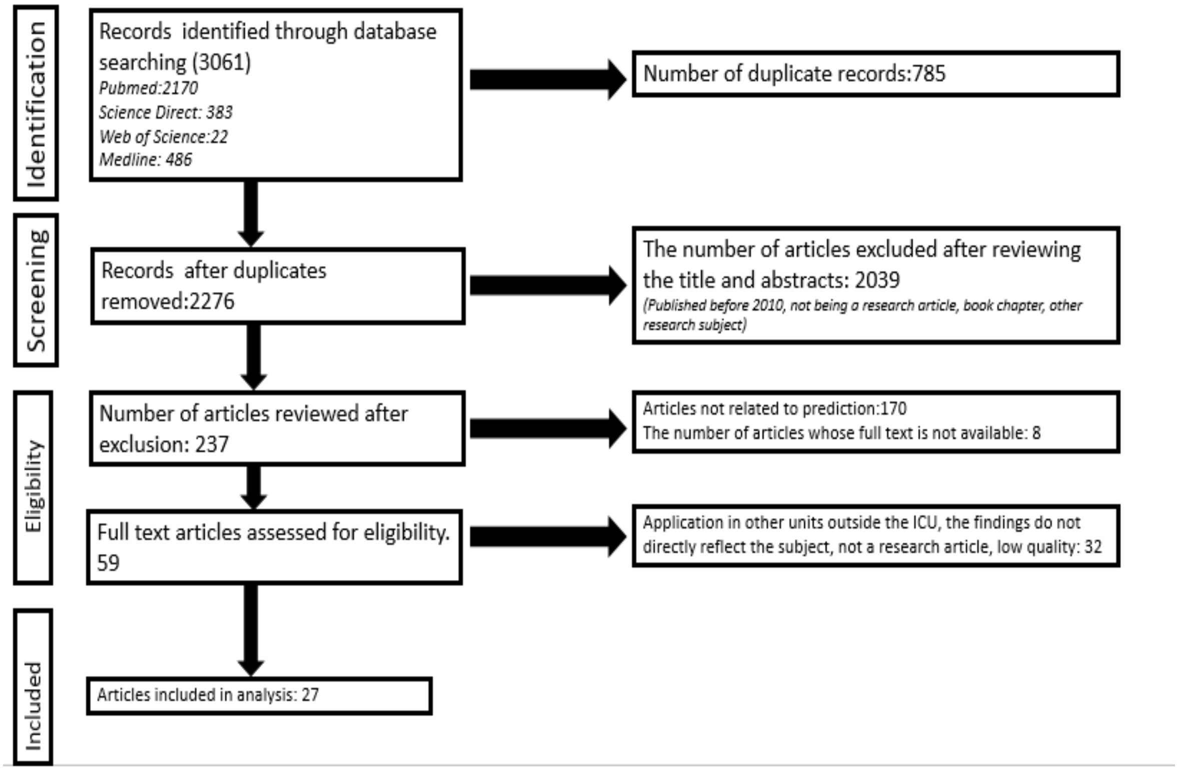

Figure 1. PRISMA Flow Chart

in this study. In addition, articles whose full text was available and evaluated as medium and high quality after quality evaluation were included in the study.

Exclusion Criteria

If the article was published before 2010, if it was a book / book section, if the authors of the publication were not reported, if the findings did not directly reflect the subject, and if the full text could not be available, the article was excluded. Articles that are not published in the English language or that are not research articles were not included.

The article was excluded in cases where the research is carried out in clinical areas other than ICU, such as the emergency department. In addition, articles determined as low quality in quality evaluation were not included in the study.

Details of the article selection process are given in Figure 1 using the PRISMA Flow Chart.

RESULTS

In this part of the study, the descriptive information and general findings of the studies included in the analysis are given. As a result of the literature search made with keywords, 3061 studies were reached. After the duplicate studies removed and screened according to the exclusion criteria, 237 articles were analysed in terms of the inclusion criteria. Articles that could not contain the full text and did not have prediction research were removed. Full text of 59 articles were reviewed. Finally, 27 articles were included in the research.

General Features of the Studies

The research consists of 27 studies conducted to predict health conditions using EHR in ICU. It was determined that the patient records varying between 100 and 121.158 were used in studies designed as single or multicentre. 16 articles were applied in the USA, 4 articles were applied in Korea, while the remaining publications were applied in UK, China, Belgium, Italy, Australia, Canada and Iran.

Articles included in the study classified according to the area to be predicted. Articles with mortality prediction models are given in Table 1, articles with sepsis prediction are shown in Table 2, pressure ulcer (PU) prediction model articles are in Table 3, articles with acute kidney injury (AKI) prediction are given in Table 4, and publications with prediction in other areas and infection are given in Table 5.

Duration of Research and Health Facilities Where Research Data are Obtained

The articles included in the study analysed 1 year to 11-year patient data.10 articles used the Medical Information Mart for Intensive Care III (MIMIC-III)

Table 1. Mortality prediction articles

	Author(s)	Health Facility	Time period	Sample	EHR-based variables	Accuracy	AUROC	Specifity
1	Marafino et al. 2018[23]	Twenty ICUs at 2 academic medical centres (University of California, Beth	January 1, 2001, through June 1, 2017	101196	Mortality, age, gender, LOS, type of ICU, vital signs and laboratory tests mortality models (APACHE IV, the Mortality Probability Admission Model III, Simplified Acute Physiology Score III)	N/A	0.922	N/A
2	Calvert et al.2016a[24]	Beth Israel Deaconess Medical Center	Undeclared	9683	Age, gender, LOS, death during hospital stay, dynamic physiological measurements with a one-hour time resolution, heart rate, pH, pulse, pressure, respiration rate, blood oxygen saturation, systolic blood pressure, temperature, and white blood cell count.	80%	0.880	81%
3	Calvert et al. 2016b[25]	Beth Israel Deaconess Medical Center	Undeclared	3054	Documented length-of-stay and survival for at least 17 h following admission. 17-h minimum accounts for a 12-hour advance warning after 5 h of patient monitoring using (The eight physiological measurements utilized with1-h resolution were heart rate, pH, pulse pressure, respiration rate, blood oxygen saturation, systolic blood pressure, temperature, and white blood cell count)	81%	0.934	80%
4	Che et al. 2017[26]	Paediatric Intensive Care Unit at Children's Hospital Los Angeles	Undeclared	398 (with acute lung injury)	Demographic information collected during admission 21 temporal variables, which possibly come from different modalities, such as injury markers, ventilator settings, blood gas values, etc. (daily recorded variables such as monitoring features and discretized scores made by experts, for the initial 4 days of mechanical ventilation)	N/A	0.789	N/A

APACHE- Acute Physiology and Chronic Health Evaluation, ICU- Intensive Care Unit, LOS -Length of Stay, SpO2-Saturation of Oxygen, PT- Prothrombin Time, PTT-Partial Thromboplastin Time

Table 1. Continued

5	Davoodi & Moradi 2018[27]	Beth Israel Deaconess Medical Center	Undeclared	10972	Age, gender, Vital sign measurements made at the bedside (~1 data point per hour) Laboratory test results (albumin, anion gap, bicarbonate, bilirubin, blood urea nitrogen, chloride, creatine, glucose lab test, haematocrit, haemoglobin, INR, lactate, mechanical ventilation, platelet, potassium, PT, PTT, sodium, temperature, white blood cell count, diastolic blood pressure, glucose, heart rate, mean blood pressure, respiratory rate, spO2, the systolic blood pressure), procedures, medications, caregiver notes, imaging reports, and mortality index (both inside and out of the hospital)	68%	0.739	68%
6	Lee et. al, 2015[28]	Beth Israel Deaconess Medical Center	Undeclared	29149	Age, gender, admission type (elective, urgent, emergency), ICU service type, primary ICD-9 code, the worst Glasgow Coma Scale, and the total urinary output from each non-overlapping 6-hour period during the first 24 hours in the ICU Vital signs every 10–15 minutes (heart rate, mean blood pressure, systolic blood pressure, SpO2, spontaneous respiratory rate, and body temperature) Lab tests results 1–4 times a day (haematocrit, white blood cell count, serum glucose, serum bicarbonate, serum potassium, serum sodium, blood urea nitrogen, and serum creatinine.) and hourly urine output measurements The receipt of vasopressor therapy during the first 24 hours in the ICU (binary), and the use of mechanical ventilation or Continuous Positive Airway Pressure during the first 24 hours in the ICU (binary),	N/A	0.753	N/A

APACHE- Acute Physiology and Chronic Health Evaluation, ICU- Intensive Care Unit, LOS -Length of Stay, SpO2-Saturation of Oxygen, PT- Prothrombin Time, PTT- Partial Thromboplastin Time

Table 2. Sepsis prediction articles

	Author(s)	Health Facility	Time period	Sample	EHR-based variables	Accuracy	AUROC	Specificity
1	Rafiei et al. 2020[29]	Beth Israel Deaconess Medical Center, Emory University Hospitals	Undeclared	40336	Age, gender, ICU LOS, SOFA, Smart Sepsis Predictor Vital signs a (heart rate, temperature, diastolic blood pressure, SPO2, systolic blood pressure, mean arterial pressure, respiration rate and the laboratory test results (serum glucose, lactic acid, FiO2, PaCO2, leukocyte count, creatinine, and	69%	0.860	69%
2	Desautels et al. 2016[30]	Beth Israel Deaconess Medical Center	2001 and 2012	40000	Age, gender, LOS, death during hospital stay, GCS Vital signs systolic blood pressure, pulse pressure, heart rate, respiration rate, temperature, SpO2	80%	0.880	80%
3	Harrison et al. 2015[31]	Mayo Clinic in Rochester	Jan 1 through Mar 31 2013;	587	Lab tests results blood or lavage, stool or urine, or fluid or sputum culture Delay in recognition and treatment (Lactate >0 Measurements Within 2 h of severe sepsis alert CVP) Systemic inflammatory response (white blood cell count, temperature, respiratory rate, heart rate) Organ hypoperfusion and dysfunction(Lactate, SBP) Shock (vasopressors, fluid resistant hypotension)	N/A	0.950	96%
4	Nemati et al. 2018[32]	Emory University Hospitals	Jan 2013 to Dec 2015;	27527	Gender, comorbidities, LOS, hospital mortality, surgery, ventilation Vital signs of the patient(heart rate, mean arterial blood pressure, respiratory rate, temperature, SpO2 and the GCS, SOFA score), AISE score (for clarity of presentation only selected time-points) Lab test results creatine, Lactate	63%	0.830	63%

AISE -Artificial Intelligence Sepsis Expert, CVP - Central Venous Pressure, EHRs-Electronic Health Records, FiO2- Fraction of Inspired Oxygen, GCS-Glasgow Coma Score, ICU- Intensive Care Unit, LOS -Length of Stay, PaCO2- Partial Pressure of Carbon Dioxide From Arterial Blood, SOFA - Sepsis-related Organ Failure Assessment

Table 3. Pressure ulcer prediction articles

	Author(s)	Health Facility	Time period	Sample	EHR-based variables	Accuracy	AUROC	Specificity
1	Cho et al. 2013[33]	University affiliated teaching hospital in Seul	Nov 2006-Apr 2007, Nov 2009-April 2010	1214	Age, gender, primary ICD-10-CM code, LOS, Vital signs, clinical measurement and observation (systolic blood pressure, ventilator mode, heart rate, body temperature, BMI, APACHE score, consciousness level, incontinence, general edema, degree of edema, number of urinations, number of self-voiding's, self-motor response, stomy, surgical operation, indwelling catheterization, hemodynamic status, other skin lesions, Braden scale, number of sedatives, number of analgesics, frequency of medication-including transfusion, iv and non iv medication) Lab test results (serum albumin, serum haemoglobin) Nursing intervations (number of positions changes, staint, TPN, diet type)	83.3%	0.850	76%
2	Cramer et al. 2019[34]	Beth Israel Deaconess Medical Center	2001 and 2012	54000	Age, gender and ethnicity. Vital signs mean arterial pressure, SpO2, GCS. Lab test results complete blood counts, electrolytes, albumin, arterial blood gases, blood urea nitrogen, bilirubin, blood glucose and INR. The patient's encoded ventilation status (no ventilation, non-invasive ventilation or mechanical ventilation, with the highest level during the first 24h used)	N/A	N/A	N/A
3	Kaewprag et al. 2017[35]	Ohio State University	Jan 1,2007 and Dec 31, 2010	7717	Age, gender, ethnicity, LOS ICD-9 code, Medication categories that appear to be significantly associated with PUs, highly associated comorbidity	N/A	0.827	90-99%
4	Hyun et al. 2019[36]	Academic medical center in central Ohio	January 1, 2007, and December 31, 2010	12654	Age, gender, LOS, weight, diabetes, vasopressor, isolation, endotracheal tube, ventilator days, ventilator episode, Braden score The body locations and categories of the HAPU (Shoulder blades, Elbow, Sacrum, Hip, Buttock, Ankle, Heel, Others, not specified)	91,7%	0,737	0,693

BMI-Body Mass Index, EHRs-Electronic Health Records, HAPU- Hospital-Acquired Pressure Ulcers, ICD-International Statistical Classification of Diseases and Related Health Problems, ICU- Intensive Care Unit, INR-International Normalized Ratio, LOS -Length of Stay, PU - Pressure Ulcer

Table 4. AKI prediction articles

	Author(s)	Health Facility	Time period	Sample	EHR-based variables	Accuracy	AUROC	Specificity
1	Koyner et al. 2018[37]	University of Chicago	Nov 2008 to Jan 2016	121158	Age, gender, ethnicity, LOS, ICU admission during stay, operating room during stay, Inpatient mortality Lab test results and Diagnostics : admission serum creatinine, admission blood urea nitrogen, receipt of dialysis > 48hr after their initial serum creatinine, location of AKI, Blood culture, electrocardiogram, echocardiography, x-ray (chest and abdomen), CT scan (with/without contrast) Interventions (IV bolus (lactated ringers, 0.9% sodium), Albumin, Mechanical ventilation) Medications (Diuretics (IV/by mouth), Nephrotoxic medications, Anti-infectives (IV/by mouth), Vasoactive, Inotropes, Insulin (IV/r subcutaneous), Hypoglycaemics (by mouth), Proton pump inhibitors) Transfusions (Packed RBCs, Frozen plasma, Platelets, Cryoprecipitate)	87%	0.960	85%
2	Sanchez & Khemani 2016[38]	Tertiary PICU (Cerner Kids database, Kansas City)	May 2003 and Mar 2015 second set Apr 1, 2012, and Mar 31, 2015	9396 children	PaO2/ FiO2 ratio, arterial oxygen saturation/ FiO2 ratio, disseminated intravascular coagulation score, and vasoactive-inotrope score Early AKI pathophysiologic groups: hemodynamic instability, hypoxemia, anaemia, inflammation, coagulopathy, liver failure, acidosis, renal/metabolic erangement, and demographics/admission characteristics.	N/A	0.840	95%
3	Xu et al. 2020[39]	Beth Israel Deaconess Medical Center	2001-2012	7657 AKI cases	Age, gender, ethnicity, Vital signs: diastolic blood pressure, glucose, heart rate, mean arterial blood pressure, respiration rate, SpO2, systolic blood pressure, and temperature. Lab test results serum creatinine bicarbonate, blood urea nitrogen, calcium, chloride, creatinine, haemoglobin, INR, platelet, potassium, PT, PTT, white blood count, the average of urine output, and eGFR that is computed by MDRD Medications: diuretics, NSAID, radiocontrast agents, and angiotensin. Comorbidities: congestive heart failure, peripheral vascular, hypertension, diabetes, liver disease, MI, CAD, cirrhosis, and jaundice.	N/A	0.775	N/A

AKI -Acute Kidney Injury, CAD-Coronary Artery Disease, CT-Computerized Tomography, EHRs -Electronic Health Records, eGFR-Estimated Glomerular Filtration Rate, FiO2- Fraction of İnspired Oxygen, ICU- Intensive Care Unit, INR- International Normalized Ratio, IV-Intra Venous, MDRD-Modification of Diet in Renal Disease, MI-Myocardial Infarction, NSAID-Non-Steroidal Anti-Inflammatory Drugs, PICU- Paediatric Intensive Care Unit, PT- Prothrombin Time, PTT- Partial Thromboplastin Time, RBC-Red Blood Cells, PaCO2- Partial Pressure of Carbon Dioxide From Arterial Blood, PaO2-Partial pressure of arterial oxygen

Table 5. Other prediction articles

	Author(s)	Health Facility	Time period	Predicted Area; Sample	EHR-based variables	Accuracy	AUROC	Specificity
1	Eickelberg et al. 2020[40]	Beth Israel Deaconess Medical Center	2001 and 2012	BIs and antibiotic therapy needs; 19633 adults	Age, gender, ethnicity Medication use (dobutamine, dopamine, epinephrine, norepinephrine, phenylephrine, renal replacement therapy, vasopressin) Vital signs, systolic blood pressure, diastolic blood pressure heart rate, SpO2, temperature, ventilation status, weight, GCS Lab test results bands, serum bicarbonate, bilirubin, blood urea nitrogen, serum chloride, creatinine, glucose, haemoglobin, INR ratio, Serum lactate, urine leukocyte, urine nitrite, PaO2/FiO2 ratio, PTT, pCO2, serum pH n/a, platelet, serum potassium, white blood cell count, serum calcium, microbiologic culture	N/A	0.800	N/A
2	Li et al. 2019[41]	University of Michigan Hospitals	Oct 2010 and Jan 2013,	Complicated CDI; 1144 cases of CDI;	Age, gender, LOS, BMI patient history within the past 90 days (e.g., diagnosis of diabetes within the past 90 days), admission details (e.g., scheduled, urgent, or emergency admission), and daily hospitalization details (prescribed inpatient medications, Day of CDI diagnosis, Charlson-Deyo score, Inflammatory bowel disease diagnosed in the past 90 da, Solid organ transplant, Concurrent non-CDI antimicrobial use, Fluoroquinolone use from admission to diagnosis, Proton pump inhibitor use, Prior CDI within the past year, Prior CDI within the past 90 d, Failed initial CDI therapy within the past 14 d)"	90%	0.840	96.7%
3	Liu et al. 2019[42]	Beth Israel Deaconess Medical Center	Undeclared	Sepsis pre-shock; 15930	Cardiovascular SOFA score; PaO2, FiO2 –Respiratory Rate; Respiratory SOFA score; Coagulatory SOFA score.	N/A	0.930	84%
4	Mollura et al. 2020[43]	Beth Israel Deaconess Medical Center	2001-2012	Septic shock 100 septic shock patients	Age, LOS, hospital and 28-days mortalities SOFA, qSOFA, co-morbidities of the included patients (congestive heart failure, Diabetes, Renal Failure, Liver Disease and the presence of coagulopathy Arterial blood pressure waveforms, availability of 1-hour recording before the septic shock onset, electrocardiogram, serum lactate, vasopressors	85%	0.930	82%

Table 5. Continued

5	Alvarez et al. 2013[44]	Dallas Parkland Hospital	18 May 2009 and 31 Mar 2010	Cardio pulmonary resuscitation and mortality; 7466	Age, gender, Vital signs, temperature, systolic and diastolic blood pressure, respiratory rate, SpO2, pulse, Lab test results (PT, PTT, potassium, glucose, haematocrit, creatinine, white blood cells, total bilirubin, sodium, arterial pH, arterial pCO2, aspartate aminotransferase, albumin, anion gap, b-type natriuretic peptide, thyroid stimulating hormone, estimated glomerular filtration rate, consciousness level, bilevel positive airway pressure, arterial blood gas, troponin I, electrocardiogram, electroencephalogram telemetry) Medication systemic steroids, sodium bicarbonate, lactulose, or rifaximin	N/A	0.850	94,3%
6	Moon et al. 2018[45]	Two university hospitals in Seoul, Korea	Sept 2009 to Apr 2012	Delirium; 3284	Age, gender, married, smoke, education, admission via emergency room, emergency room length of stay, ICU LOS, Ramsay sedation score, sleep disturbance, mechanical ventilation, oxygen use, level of conscious score, last pulse rate before developing of delirium, activity (dependent), BUN, infection, total numbers of catheters, restraints	1 Year 78%	1 Year 0.850	1 Year 75%
7	Lee et al. 2018[46]	A tertiary care teaching hospital	Jul 1, 2013, and Jun 30, 2016	Unplanned extubation; 302016 adults	Age, weight, APACHE, Vital signs and lab test results systolic blood pressure, mean blood pressure, diastolic blood pressure, pulse rate, respiration rate, body temperature, SPO2, urine amount, glucose Other: Minute volume, patient position (head up vs. others), Presence of restraint (yes vs. no), ventilator mode (spontaneous vs. control), PIP, minute volume, urine volume Features with ≤3 records: (GCS, Richmond Agitation and Sedation Scale, Motor power of arm, motor power of leg, Fio2, PEEP, E-tube depth, E-tube ID)	N/A	Model 1-2-3 0.880, 0.880, 0.900	Model 1-2-3 94%, 91%, 92%
8	Jeong et al. 2018[47]	South Korea Asian Medical Center	Jan 2011 and June 2017	28-Day Mortality in Patients with Sepsis; 482 adult patients with sepsis;	Age, gender, height, BMI, comorbidities, diagnosis, LOS, mechanical ventilation, Vasopressor use, and renal replacement therapy (RRT, APACHE II score, SOFA score, respiratory disease, liver/gı disease, cardiovascular disease, renal disease, febrile neutropenia, SSTI, Other the NUTRIC score (0–10) and modified NUTRIC score (0–9)	N/A	0.762	65%

Table 5. Continued

9	Meyfroidt et al. 2011[48]	Leuven University Hospitals	Jan and the 4 Dec 2007, and second period Mar 2008 and 8 Jan 2009	Discharge after cardiac surgery; 960	ICU LOS, ICU mortality, hospital mortality, Euroscore, type of surgery, repeated cardiac surgery, post-endocarditis Admission data including the patient's history and preoperative medical condition, the day of the week, and demographic data. Vital signs: systolic arterial blood pressure,SpO2, heart rate, central blood temperature, and systolic pulmonary artery pressure Medication data: type and cumulative dosage of drugs, intravenous fluids and blood products used during the first 4 hours in the ICU. Laboratory data of the first 4 hours in the ICU. Physiological data: monitoring data mechanical ventilator data, blood loss, and urine output, registered during the first 4 hours in the ICU.	N/A	0.700	N/A
10	Bose et al. 2019[10]	Johns Hopkins All Children's Hospital	11 Jan 2013-16 Sept 2015	Neonatal cardiac arrest; 22 cardiac arrest and 206 control patients ≤1-year-old;	Age, heart rate, age- and sex-adjusted respiratory rate SpO2, Premature ventricular contraction rate, Heart rate variability - heart rate variability - low frequency power and band power Heart rate variability - high frequency power in the high frequency band power, ratio of heart rate variability of high frequency power	70.8%	0.910	74.1%

APACHE- Acute Physiology and Chronic Health Evaluation, BI- Bacterial Infections, BMI-Body Mass Index, CDI- Clostridium Difficile Infection, EHRs -Electronic Health Records, FiO2- Fraction of Inspired Oxygen, ICU- Intensive Care Unit, LOS- Length of Stay, NUTRIC- Nutrition Risk in the Critically, PaO2-Partial Pressure of Arterial Oxygen, pCO2- Partial Pressure of Arterial Carbon Dioxide, PTT-Partial Thromboplastin Time, SOFA - Sepsis-related Organ Failure Assessment, SSTI-Skin and Soft Tissue Infection, UE - Unplanned Extubation.

database, which is a defined and publicly available data set containing healthcare data from approximately sixty thousand patients.

Research has been conducted at Parkland Hospital, Johns Hopkins All Children's Hospital; Beth Israel Deaconess Medical Center (BIDMC), University of Chicago, Los Angeles Children's Hospital, University of Michigan, Ohio State University, University of California, San Francisco Leuven Hospitals; Emory University Hospitals, Kansas Cerner Kids University Center, university affiliated teaching hospital in Seoul, academic medical center in central Ohio; Asian Medical Center South Korea.

Score/Algorithm/Scale/Model Used for Model Validation

The prediction models developed as a result of the studies have been validated with Acute Physiology and Chronic Health Evaluation (APACHE) IV, the Mortality Probability Admission Model III, Modified Early Warning Score (MEWS), Simplified Acute Physiology Score (SAPS II and III), Sequential Organ Failure Assessment (SOFA), Receiver Operating Characteristic (ROC), Lung Injury Score (LIS), Oxygenation Index (OI), Mean Airway Pressure (MAP) and peak inspiratory pressure (PIP), Naïve Bayes (NB), decision trees (DT), Gradient Boosting (GB), Deep Belief Networks (DBN) classification and scoring systems.

Variables Used

The use of some variables has come to the fore in the process of developing algorithms to predict possible adverse health conditions or poor outcomes in the patient that can be used in risk management. The variables considered in algorithms can be examined in five groups. The variables used in estimation models are classified as demographic variables, variables related to vital sign measurements, laboratory results, variables specific to the prediction area and other variables, and are given below.

General variables: Age, gender, ethnicity, length of stay (LOS), 28-days mortalities, survival for at least 17 h following admission, admission type (elective, urgent, emergency), ICU service type, mechanical ventilation day.

Vital sign variables: Temperature, heart rate, mean blood pressure and arterial pressure, respiratory rate, spO2, the systolic/diastolic blood pressure, hourly urine output.

Laboratory test variables: Albumin, anion gap, bicarbonate, bilirubin, BUN, chloride, creatine, haematocrit, haemoglobin, WBC, INR, lactate, platelet, potassium, PT, PTT, sodium, glucose procedures, blood culture.

Variables Specific to the Prediction Area

Sepsis specific variables: blood, lavage, stool, urine, fluid and sputum culture order, central venous pressure (CVP), fraction of inspired oxygen, comorbidity (congestive heart failure, diabetes, renal failure, liver disease), presence of coagulopathy, electrocardiogram, availability of 1-hour recording before the septic shock onset, partial pressure of carbon dioxide from arterial blood (PaCO2).

PU specific variables: Body Mass Index, hemodynamic status, consciousness level, incontinence, general edema, degree of edema, number of urinations, number of self-voiding's, self-motor response, indwelling catheterization, stomy, surgical operation, other skin lesions, braden scale, nursing interventions (number of positions changes, staint, TPN, diet type), the categories of hospital-acquired PU s (shoulder blades, elbow, sacrum, hip, buttock, ankle, heel, others, not specified), comorbidity.

Acute Kidney injury (AKI) specific variables: Receipt of dialysis > 48hr after their initial serum creatinine, location of AKI, transfusions (Packed RBCs, Frozen plasma, Platelets, Cryoprecipitate), diagnostics (Electrocardiogram, Echocardiography, x-ray (chest/abdomen), CT scan (with/ without contrast), pathophysiologic groups for Early AKI: hemodynamic instability, hypoxemia, anaemia, inflammation, coagulopathy, liver failure, acidosis, renal/metabolic erangement, the Risk-Injury-Failure-Loss-End criteria, then paediatric RIFLE criteria, the Acute Kidney Injury Network criteria, the Kidney Disease: Improving Global Outcomes criteria, the minimum value of estimated glomerular filtration rate that is computed by Modification of Diet in Renal Disease

Other variables: Medications (number of sedatives/analgesics/ psychopharmacology drugs, frequency of medication-including transfusion/iv-noniv medication, dobutamine, dopamine, epinephrine, norepinephrine, phenylephrine, renal replacement therapy, vasopressin, IV bolus (lactated ringers/0.9% sodium), albumin, diuretics (IV/by mouth), Nephrotoxic medications, anti-infectives (IV/by mouth), vasoactive, insulin, hypoglycaemics, proton pump inhibitors, caregiver notes, imaging reports, and mortality index, ventilator days, primary diagnosis (ICD-10-CM code), minute volume, urine volume, Features with ≤3 records: (GCS, RASS, Motor power of arm, Motor power of leg, PIP, PEEP, Weight, E-tube depth, E-tube ID), ramsay sedation score, sleep disturbance, last pulse rate before developing of delirium, activity (dependent), psychopharmacology drugs, patient history within the past 90 days, admission details (e.g., scheduled, urgent, or emergency admission), and daily hospitalization details (prescribed inpatient medications, day of Clostridium difficile infection (CDI) diagnosis, Charlson-Deyo score, inflammatory bowel disease diagnosed in the past 90 days, solid organ transplant, concurrent non-CDI antimicrobial use, fluoroquinolone use from admission to diagnosis, proton pump inhibitor use, prior-CDI within the past year/90 days, failed initial CDI therapy within the past 14 days.

DISCUSSION

27 articles that developed algorithms using AI technologies to predict adverse health conditions using EHR in the ICU were included in the systematic review. It has been found that EHR-based prediction models are good risk management and decision support tools and adoption of such models in ICUs may reduce the prevalence of adverse conditions. It has been reported that data-based risk assessments and prediction of adverse conditions can be used to improve quality in patients treated in the ICU and will help clinicians to improve patient care.

Mortality Prediction Articles

The most unfavourable situation and the most important risk for a patient who receives health services in the ICU is death. Analysing and evaluating patients in terms of mortality risk, determining the risk level and intervening according to the analysis results will provide healthcare professionals with an opportunity to reduce undesirable situations. Six articles on predicting mortality risk are included in this review. 4 of these publications are about the models created by using the MIMIC database obtained from inpatients at the "BIDMC Medical Intensive Care Unit". One publication was applied to paediatric patients with acute lung failure and the other was to Alcohol Use Disorder. The last publication was multicentred with the participation of 20 ICUs.

The articles use Logistic Regression (LR), Decision Trees (DT) and Gradient Boosting Trees (GBT), Linear Support Vector Machine (SVM), deep network models as deep feed-forward neural network and mimic learning models for ML.

In the study conducted by Marafino et al. (2018), two generalizable and validated modelling approaches were developed. The models predict inpatient mortality better by using the patients' first 24-hour data after hospitalization to the ICU. The model achieved an AUC of 0.922 compared with 0.88 reported for APACHE IV, 0.85 for the Simplified Acute Physiology Score III, 0.82 for the Mortality Probability Admission Model III. It has been reported that the developed model can be adapted to EHRs and can be used by healthcare professionals for risk adjustment, quality improvement initiatives and many other purposes in clinical studies.

It has been found that the model named AutoTriage gives better results with an AUROC value of 0.934 for12-h mortality prediction, in the sensitivity of 90% and specificity of 80% than existing prediction methods and also shows improvements in both accuracy and Odds Ratio compared to existing methods in patients with alcohol use disorder (24,25).

Che et al. (2017) reported using knowledge distillation approach with gradient boosting trees model. The approach was called interpretable mimic learning. Test results on Paediatric ICU dataset for acute lung injury demonstrated that mortality and ventilator-free day prediction performance of the developed model is better than the state-of-the-art approaches (AUROC score of 0.7898). It has also been determined that the model can identify important features/markers in predicting mortality and days without a ventilator. Another proposed model for predicting mortality in ICUs, the Deep Rule-Based Fuzzy System has been proven to outperform various methods while preserving interpretable rule bases. The developed model used fuzzy clustering to address the problem of the methods' inappropriateness for large databases and insufficient repeatability. The specificity (68.12%), sensitivity (68.14%) and AUROC (0.739) criteria, which are obtained by the proposed method, indicated that DRBFS can not only predict true mortality rates but also avoid false mortality indexing survived patients. (27).

In mortality risk analysis, it has been determined that using subsets of similar patients instead of a heterogeneous population improves prediction performance and the use of more similar patients leads to an increase in the performance of the prediction model due to increased homogeneity. The maximum AUROC of 0.753 was achieved with 2000 most similar patients. It has been argued that LR is the model with the best predictive performance. However, it was emphasized that if the sample size is small, the forecast performance decreases over time (28).

Sepsis Prediction Articles

One of the unintended consequences of patient care or treatment in ICUs is the development of infection in the patient and one of the most serious symptoms is the development of sepsis. The number of reliable and intelligent systems used in sepsis prediction is limited. However, for the survival of patients at risk of developing sepsis, assessment of the risk and early prediction of the onset of sepsis provides an opportunity for early intervention. (29) Sepsis prediction was performed in 4 of the publications included in this study.

The study conducted by Nemati et al. (2018) used MIMIC III database, demonstrated preferable performance of a sepsis prediction model called Artificial Intelligence Sepsis Expert (AISE) over incrementally longer time windows. In sepsis prediction, the AISE algorithm was better than tSOFA in the same time window and remained superior up to 12 hours. It is validated that AISE could accurately predict the onset of sepsis 4 to 12 hours prior to clinical diagnosis by using real-time EHR data in the ICU in. AISE achieved AUROC in the range of 0.83–0.85, specificity of 63%, accuracy of 63% at a prediction window of 12 hours.

In the patients with severe sepsis, the lactate level and the lack of CVP measurement on time were determined as the cause of optimized delay in the diagnosis and treatment component. Infection suspicion, SIRS positivity and low systolic blood pressure were determined as the biggest predictive value in sepsis risk assessment and prediction. In the study an algorithm had been developed to predict sepsis based on organ hypoperfusion and dysfunction, systemic inflammatory response syndrome, criteria for suspicion of infection and shock. When applied to the validation cohort, it was determined that the algorithm has 80% sensitivity and 96% specificity and AUROC 0.950 (31).

It has been determined that InSight which can be integrated into the EHR system autonomously, shows better results than SAPS II and SOFA (AUROC 0.880, accuracy 80% and specificity of 80%) It performs well even with randomly missing data without the need for any additional data collection and also superior to the qSOFA and SIRS that use similar data for calculation (30).

Rafiei et al. (2020) developed and validated a sepsis prediction algorithm called Smart Sepsis Predictor (SSP) by using 2019 PhysioNet/Computing in Cardiology Challenge dataset. It has been reported that SSP is a high-performance ML-based system. The results show that SSP robust to data deficient and extreme values and can make accurate predictions in case of errors and achieving an AUROC of 0.86, accuracy of 69%, specificity of 69% for 12 hours before sepsis onset. According to the article, the results and the comparative plots has been shown that SSP performed better in predicting the onset of sepsis compared to models such as AISE or InSight.

Pressure Ulcer Prediction Articles

PU s have a serious negative effect on patient healing and also puts a serious burden on the health system. Due to the increase in the incidence of infection, sepsis and additional surgical procedures, LOS takes longer and hospital costs increase (36). Considering the high cost of treatment of PUs and its strong negative impact on the patient, PU risk analysis is invaluable. Researches concluded that working with a large database derived from ICUs allows the characteristics of patients who develop pressure ulcers while staying in the ICU, to make comparisons with patients without PUs and to develop a prediction model based on these data. The studies in this field reported that proposed PU prediction models achieved AUROC in the range of 0.82–0.85. EHR-based PU prediction models would assist clinicians in risk assessment and can be easily adapted to clinical applications due to its easy interpretation so that they are good risk management and decision support tools (34,36). Using PU predictive model reduced the prevalence tenfold and the ICU LOS by about one-third and increased data entries regarding ulcer severity and body site. These models were found to have higher performance and better selectivity than Braden score and predict future PU development in 24 hours (33,34,36).

The study that use all combinations of Bayesian Network (BN) models identified strong relationships between risk factors (Braden total score, diabetes, malnutrition etc.) generally considered as associated with PUs. This prediction model provides evidencebased risk assessment and a better understanding of risk factors, enabling protective measures to be taken (35).

AKI Articles

AKI is a critical clinical event manifested by an abrupt decrease of renal function, affecting more than 50% of patients admitted to the ICU. (39,49) AI based AKI prediction models are good risk management tools. These models can be used to identify patients with high risk of developing severe AKI accurately. The studies concluded that models predict whether a patient develops AKI within 7 days or requires rapid intervention at least 1-2 days before and the prediction models achieved AUROC in the range of 0.77–0.96 for adult patients and 0.84 for paediatric patients (37,39).

Another study was conducted in the paediatric ICU and Paediatric Early AKI Risk Score was developed and the scoring was validated. It was concluded that an AKI clinical prediction model based on the developed data has good separation and calibration in the paediatric ICU population (38) The feature of the model is that it makes predictions using EHRs that can be obtained in real time during the first 12 hours in the ICU and can be generalized to paediatric ICUs. This prediction model can be applied to guide ICU service strategies and as a clinical decision support system.

Other Prediction and Infection Articles

In 10 studies included in the research, conditions such as infections, delirium, unplanned extubation, cardiopulmonary resuscitation and mortality, neonatal cardiac arrest, 28-day mortality in patients with sepsis, discharge after cardiac surgery have been estimated.

Bacterial infections (BI) are common in ICUs and have a fatal course. Infections increase LOS and healthcare costs. Additionally, infections nowadays are considered as a major cause of morbidity and mortality (50). According to SAS, it is necessary to evaluate the infection risk in terms of patient and employee safety in all areas and processes where health services are provided and to take necessary measures and ensure their continuity (8). EHR based BI prediction models provide the opportunity to accurately identify patients at risk of infection. BI prediction model developed by Eickelberg et al. (2020), identified patients with low BI risk who would benefit from discontinuation of empirical antibiotic therapy within 24 hours from the beginning. The developed model identified patients at low risk of BI with AUROCs up to 0.8 and negative predictive values >93% (40).

In the study conducted by Li et al. (2019), the effect of ML approach using EHR data in determining the risk stratification of developing complications in patients was investigated. A model was developed to predict Clostridium Difficile Infection (CDI) that achieved an AUROC of 0.84 and the specificity of 95.3%. Using the EHR data, it has been determined that CDI cases can be classified according to the risk of developing complications. EHR-based models based on thousands of variables provided better risk predictions compared to other sets. Although such models do not identify new risk factors, it has been reported that they consider a much wider set of patient characteristics than any clinician could examine simultaneously.

Prediction of mortality in patients with sepsis is the focus of the study conducted by Jeong et al. (2018). The study was conducted to compare the accuracy of the Nutrition Risk in the Critically (NUTRIC) Score and the modified NUTRIC Score in predicting 28-day mortality in patients with sepsis. The analysis showed that patients with a high NUTRIC score and a high modified NUTRIC score had increased 28-day mortality, and both scores were a good predictor of 28-day mortality in septic patients. AUROC. sensitivity and specificity of the NUTRIC Score for predicting 28-day mortality was 0.762-79% - 60% and of the modified NUTRIC Score 0.757-75%- 65%.

Risk assessment of sepsis and septic shock was the focus of the study conducted by Liu et al (2019). The developed model was reported to be successful in determining patients with sepsis who are likely to develop septic shock and makes it possible to intervene in the early hours before septic shock develops. With the method determined to be the best, an average early warning time of 7 hours were reached and achieved a 0.93 AUROC, 88% sensitivity, 84% specificity for identifying patients with sepsis who will progress to septic shock. Another AI based model demonstrated that to predict 15 minutes before whether a patient will develop septic shock in the patient using the 45-minutes record of vital signs (AUROC 0.930, accuracy 85%, specificity 82%). According to results blood pressure plays a key role in identifying patients with shock, and the availability of instantaneous features is important to characterizing the physio pathological mechanisms that lead to shock (43).

In the study conducted by Moon et al. (2018), a delirium risk scoring algorithm called Auto-DelRAS was developed. It has been reported that the Auto-DelRAS model facilitates the identification of ICU patients at high risk for delirium development and has the potential for nurses to initiate preventive delirium interventions in a shorter time. The one-year predictive validity of Auto-DelRAS was reported as a sensitivity of 0.88, specificity of 0.72, a positive predictive value of 0.53, and a negative predictive value of 0.94 and AUROC of 0.850.

Another study has been conducted to predict unplanned extubation in ICUs. Three prediction models have been developed. AUROC of models 1-2-3 were 0.880, 0.880, 0.900 and specificity 94%, 91%, 92% respectively. Combining the GCS, minimum pulse and respiratory rate, and PIP values, and the frequency of patient status assessment recording, the minimum respiration rate and patient positioning was found to be the model with the highest sensitivity in terms of predicting unplanned extubation (46).

1/100 of hospitalized patients experienced resuscitation events, and death events, one of the most serious of all adverse patient safety outcomes. Computer-based predictive models for determining the risk of resuscitation events, and death can be an effective tool to reduce cardiopulmonary arrest and unplanned transfers to the ICU. The EHR-based cardiopulmonary arrest and mortality prediction model developed by Alverez et al. (2013) was better at predicting serious poor outcomes compared to previously developed risk models (AUROC 0.850, specificity 94%) and the "human judgment-based Rapid Response Team" approach. Similar models used in risk estimation in ICU will provide more effective and meaningful use of EHRs to improve inpatient outcomes. In another study conducted by Bose et al. (2013), a model for early prediction of impending cardiac arrest was developed using physiological data in neonates and infants with heart disease receiving treatment in the cardiovascular ICU. As a result of the study, it was found that the prediction model using physiological follow-up data of new-borns and infants with heart disease hospitalized in paediatric CVC ICU can determine the approaching cardiac arrest an average of 17 hours before cardiac arrest with an overall accuracy of 75%, the sensitivity of 61%, specificity of 80%, and AUROC of 0.910.

Meyfroit et al. (2011) aimed to develop a model that predicts the discharge of non-emergency cardiac surgery patients from the ICU by analysing the first 4-hour data in EHRs. It has been reported that the prediction model developed as a result of the research using Gauss processes, which is a ML technique, correctly predicts the probability of discharge from the ICU on the day after surgery and the day of discharge achieving AUROC of 0.700. The Gaussian process model predict significantly better than EuroSCORE and nurses and has been reported to perform at least as well as ICU physicians.

CONCLUSION

This systematic review brought together researches on prediction models developed by artificial intelligence in ICUs using EHRs. It was concluded that the 27 articles included in the study were conducted on mortality, sepsis, PU, AKI, cardiopulmonary arrest, delirium, discharge and unplanned extubation. The use of EHRs generated during healthcare and consisting of big data stores offers opportunities to develop new predictive models that can be used as clinical decision-making tools. It has been reported that data-based risk assessments and prediction of adverse conditions can be used to improve quality of health care in the ICU, and will help clinicians improve patient care. It has been found that AI based prediction models are good risk management and decision support tools, and adoption of such models in ICUs may reduce the prevalence of adverse conditions.

Also, the article results remark that developed AI models was found to have higher performance and better selectivity than previously developed risk models/scores, so they are better at predicting risks and serious adverse events when used in ICU. In conclusion, for improving healthcare quality and clinical outcomes in ICUs, it is recommended to use AI based prediction models developed using EHRs in risk management studies, and to enhance researches in different health conditions.

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