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COVID-19 screening: Combining AI and rapid blood diagnostics during emergency care

There is an urgent call for hospitals to triage COVID-19 more rapidly and accurately to minimise the spread of infection. CURIAL, an AI-driven triage tool developed independently by the University of Oxford, leverages routine clinical data – such as vital signs and complete blood count – collected at the point of care to rule out COVID-19 within an hour of patients arriving at a hospital emergency department.

Support for the development of this article was provided by Sight Diagnostics

In emergency departments (EDs), rapid and accurate COVID-19 screening is critical for effective infection control and ensuring timely – and appropriate – delivery of care for patients. With the pandemic relentlessly exerting an unprecedented burden on the healthcare system worldwide, this call for fast identification of COVID-19 at the point of care is more urgent than ever.

Currently, the nasopharyngeal swab RT-PCR test - the gold standard for SARS-CoV-2 testing - has a few limitations, including a long turnaround time (12-24 hours), limited sensitivity and requiring laboratory infrastructure.¹ The rapid lateral flow antigen detection test yields results faster, but has other limitations such as poor sensitivity. For example, in a study in Liverpool, the overall sensitivity of the rapid test was only 40.0%, i.e., the test only detected four in 10 people who tested positive by PCR.² And due to this risk of false results and imprecisions in the manufacturer's accuracy claims, the US Food and Drug Administration recalled and withdrew the rapid tests from sale in the US in June 2021.3

Because it is vital to make quick decisions about a patient's care pathway (admission, treatment approach, discharge, etc.) while keeping the hospital environment safe, there is a system-wide operational and safety impact when effectively performing front-door COVID-19 triage in the ED.

Leveraging artificial intelligence (AI) for faster COVID-19 screening

The CURIAL algorithm – developed by infectious disease and machine learning experts at Oxford University – is a viable alternative to traditional testing that can successfully rule out COVID-19 within the first hour of a patient's arrival at an emergency department. The CURIAL AI algorithm uses the data from routine CBCs, urea and electrolyte tests, vital signs, liver function tests, C-reactive protein (CRP) tests and blood gas to predict the probability of a patient testing positive for COVID-19.⁴

Therefore, to combat the transmission of SARS-CoV-2 while providing high-quality care

to patients – all within a reasonable timeframe – CURIAL can be an effective, and faster, solution to triage patients for COVID-19 in the ED setting.

CURIAL data and model accuracy

CURIAL developed two models to predict COVID-19 in patients: The ED model (for all patients visiting the ED) and the admissions model (for subsequently admitted patients). The training data, gathered from four teaching hospitals in Oxfordshire, assessed 155,689 adult patients at Oxford University Hospitals between 1 December 2017 and 19 April 2020. When calibrated during training to a sensitivity of 80% - the ED model attained 77.4% sensitivity and 95.7% specificity for identifying COVID-19 patients among all patients presenting to hospital. And correspondingly - with the same calibration - the admissions model achieved 77.4% sensitivity and 94.8% specificity. In terms of negative predictive values (NPVs) - the probability that patients with a negative result truly don't have COVID-19 - both models achieved high NPVs (>98.5%) across a range of prevalences (≤5%), allowing for a quick and reliable rule-out.

During a real-world evaluation of the CURIAL models over a two-week test period (20 April-6 May 2020) in Oxford University Hospitals' EDs, CURIAL displayed impressive accuracy. The ED model (3326 patients) achieved 92.3% accuracy (NPV 97.6%), and the admissions model (1715 patients) achieved 92.5% accuracy (NPV 97.7%) in comparison to PCR results.⁴

Using point of care diagnostics alongside AI

To understand which individual features had the most significant influence on model predictions, CURIAL ran a relative feature importance analysis. For both models, eosinophils and basophils had most significant effects on model performance,⁴ meaning complete blood counts directly impact the CURIAL algorithm's success.

As effective AI-powered COVID-19 screening relies on time-sensitive and accurate CBC results, the University of Oxford researchers created a version of CURIAL, called

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5 Mageit S. Oxford University Hospital deploys blood analyser as part of COVID screening [internet]. Mobi Health News 2021; March 15. www. mobihealthnews.com/news/ emea/oxford-universityhospital-deploys-bloodanalyser-part-covidscreening (accessed Oct 2021). CURIAL-Rapide, that leverages only CBC results and vital signs to screen for COVID-19 in patients. Consequently, CURIAL-Rapide creates a new collaborative pathway where point of care CBC analysers – such as Sight Diagnostics' OLO haematology analyser – are used in conjunction with CURIAL to potentially further expedite the overall screening turnaround time. And when the analyser can provide rapid results with lab-grade accuracy – OLO produces accurate results in approximately ten minutes – it can play a pivotal role in ensuring a safer hospital environment by triaging COVID-19 patients efficiently. For example, by reconfiguring the care pathway and removing the time and logistical constraint of using conventional lab infrastructure, hospitals can create separate areas (hot-labs) for CBC testing before patients enter EDs to reduce operational strain and staff work time while keeping the hospital safe from COVID-19 transmission.

To substantiate this innovative pathway and the CURIAL-Rapide algorithm, the University of Oxford deployed OLO analysers at the John Radcliffe Hospital in February 2021 to power lab-free screening. The study's interim evaluation was successfully completed, and results will be published soon.

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Having accurate CBC results in minutes, from OLO, would help CURIAL-Rapide make predictions even sooner, potentially reducing care delays and supporting infection control within hospitals. Our goal is to get the right treatment to patients sooner by helping rule out COVID at triage for a majority of patients who don't have the infection. This project shows that artificial intelligence can work with rapid diagnostics to help us select the best care pathways and minimise risks of spreading the infection in hospitals.⁵

Andrew Soltan, academic clinician and machine learning researcher at Oxford University

TABLE 1

Prevalence of COVID-19 in test set

PPV and NPV of the ED and admissions models, calibrated during training to 70% and 80% sensitivities, for identifying COVID-19 in test sets with various prevalences.⁴ From Lancet Digit Health 2021;3(2):e84.

	1%	2%	5%	10% *	20%**	25%	33%	50%
ED model								
Sensitivity 0.70								
PPV	0.203	0.383	0.613	0.763	0.834	0.902	0.888	0.979
NPV	0.996	0.990	0.985	0.953	0.932	0.871	0.886	0.778
Sensitivity 0.80								
PPV	0.133	0.282	0.493	0.638	0.767	0.831	0.823	0.944
NPV	0.997	0.993	0.991	0.962	0.946	0.909	0.908	0.820
Admissions model								
Sensitivity 0.70								
PPV	0.175	0.304	0.513	0.595	0.830	0.859	0.876	0.950
NPV	0.996	0.992	0.982	0.969	0.926	0.905	0.881	0.785
Sensitivity 0.80								
PPV	0.098	0.211	0.390	0.509	0.755	0.797	0.812	0.922
NPV	0.998	0.994	0.986	0.977	0.942	0.920	0.907	0.841

ED: emergency department. NPV: negative predictive values. PPV: positive predictive values. *The 10% scenario approximates the observed prevalence of COVID-19 in patients presenting to the study hospitals during 1–8 April 2020. **The 20% scenario approximates the observed prevalence of COVID-19 in patients admitted to the study hospitals during 1–8 April 2020.

FIGURE 1 Relative importance of features for the ED and admissions models

ALT: alanine aminotransferase. APTT: activated partial thromboplastin time. CRP: C-reactive protein. ctO2c: calculated oxygen content. ED: emergency department. FCOHb: fraction of carboxyhaemoglobin. p50c: calculated pressure at which haemoglobin is 50% bound to oxygen.⁴ From Lancet Digit Health;2021;3(2):e83.



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Blood test essinophis

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Sight OLO® performs with high accuracy for all CBC parameters

Blood 985 mettaemoglobin

Blood test monocytes

vital sons respiratory rates

Blood rest white cells

Sight OLO haematology analyser streamlines the typical blood staining workflow while maintaining lab-grade accuracy. Through a quick finger prick and the culmination of cutting-edge innovations in physics, optics, sample preparation, and an Al-based computer vision algorithm, the self-contained quantitative multi-parameter analyser can deliver fast and accurate CBC results within minutes in point of care settings.

During a recent study, the accuracy of OLO

was compared with the Sysmex XN-1000 System. Samples - covering a broad clinical range for each tested parameter - from 355 males (52%) and 324 females (48%) aged 3 months to 94 years were analysed. The regression analysis results showed a consonance in correlation coefficient and slope, bias and intercept between OLO and Sysmex XN. Therefore, the study concluded that OLO performs with high accuracy for all CBC parameters,6 thus, making OLO the perfect partner to use alongside an AI COVID-19 screening initiative, such as CURIAL.

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FIGURE 2

Meta-analysis plot graphs displaying the results of a method comparison study between the Sight OLO and the Sysmex XN haematology analysers. Graphs indicate Pearson correlation, slope and bias for each parameter *From AJH 2021;96(10):1269*.



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Sight OLO^{*} haematology analyser



Proven lab-grade results without the lab

OLO provides 5-part CBC results with 19 parameters and sophisticated flagging capabilities at the point of care. In addition, it is the first CBC analyser that is FDA 510(k) cleared for blood taken directly from either a finger prick or a venous sample for patients aged three months and above.

Finger prick sampling option

Each test requires just two drops of blood from a finger prick, which is beneficial in fast-paced emergency care settings. In addition, this functionality of processing finger prick samples makes OLO accessible to babies, elderly patients and mental health patients – so even the most sensitive patients in delicate situations can get precise results.

Delivers results in minutes

The sample preparation process is under one minute, with the full results ready in minutes. Therefore, when used in conjunction with CURIAL, OLO can help determine patient care pathways within 30 minutes.

Ideal for EDs, critical care settings, field hospitals and remote clinics

OLO is perfectly suited for point of care settings as it has a small footprint (284mm x 254mm x 323mm) and can be placed on any stable surface. It uses a disposable cartridge per test, eliminating the need for reagent management or liquid waste disposal.

Simple to set up and maintain

OLO comes factory calibrated for a quick set-up, requires only a power outlet, and needs no maintenance or manual quality control. As OLO requires no calibration by a specialist and uses disposable kits with zero washouts, the ED's operational efficiency increases, cost overheads decrease, and medical staff can focus on providing high-quality patient care.

Easy to operate

It is easy to use and designed for high-paced environments like emergency departments, with minimal training required. Its step-by-step on-screen guidance is designed for operators with any level of experience.

OLO is CE Marked according to the IVD European directive for performing CBC tests in point of care settings. The device is also FDA 510(k) cleared for use in moderately complex settings in the United States. For full indication for use and safety information, please visit the Quality and Compliance page at www.sightdx.com.

Learn more about CURIAL's rapid identification of COVID-19 and CBC results' role in improving ED patient flow in a Sight Diagnostics CURIAL webinar. Register at www.sightdx.com/events/curial-rapide to watch the full webinar.

Higher in-hospital mortality risk with anticoagulant use at time of major trauma normalises over six months

A study has found that while anticoagulant/ antiplatelet use in older, major trauma patients increases their risk of in-hospital mortality, six months later, there was no adverse effect of these drugs on functional outcomes.

The main use of anticoagulant drugs is to prevent thromboembolic events linked with atrial fibrillation, mechanical heart valves and deep vein thrombosis. Although anticoagulants are an effective form of treatment, the drugs are associated with an increased risk of bleeding. Moreover, the proportion of older patients experiencing major trauma has doubled from 2007 to 2016, increasing by around 4.3% per year and attributable to a greater number of falls and transport-related events.1 While greater use of anticoagulants such as warfarin has been shown to be an independent predictor or mortality in trauma patients,² other data have not supported this conclusion.³ Furthermore, there are few data on the long-term outcome of trauma patients prescribed anticoagulants.

With such a lack of data, a team from the School of Public Health and Preventative Medicine, Monash University, Melbourne, Australia, sought to quantify the association between anticoagulant and antiplatelet use and the short- and long-term outcomes in older patients with major trauma.⁴ They included all older (defined as 65 years and older) hospitalised trauma patients from 2017 to 2018 and retrieved the information from the Victorian State Trauma System (VSTR), a populationbased registry that collects data on all hospitalised trauma patients in Victoria, New South Wales, Australia. Using the VSTR, the researchers included patients who met the following inclusion criterion: death due to injury, higher injury severity scores (> 12 on the Abbreviated Injury Scale), admission to intensive care for more than 24 hours and requiring mechanical ventilation for part of their stay, urgent surgery, 20-29% total body surface area partial or full thickness burns. The team also extracted drug information, including those prescribed either an anticoagulant or antiplatelet, categorising patients as: anticoagulant users, antiplatelet users and non-anticoagulant users. Groups were compared in terms of in-hospital mortality, length of hospital stay and Extended Glasgow Outcome Scale (GOS-E) at six months after their injury. The GOS-E categories patient



function into eight different categories, with upper values indicating good recovery.

Findings

A total of 1323 patients were eligible for inclusion in the study, of whom 18.8% were prescribed anticoagulants and 28.7% antiplatelets. Among those taking anticoagulants, the majority (45.8%) were aged 75-84 years of age and 59.4% were males. The most common major trauma was a subdural haematoma (45.6%). In-hospital mortality was 31.7% among those taking anticoagulants and after adjustment for age and various other factors, the risk of in-hospital mortality was significantly higher compared with the nonanticoagulant group (odds ratio, OR = 2.38, 95% CI 1.58-3.59). Similarly, the adjusted odds ratio for those prescribed antiplatelets was also higher than non-users, although the difference was not significant (OR = 1.12, 95% CI 0.74-1.71). When comparing the GOS-E at 6 months, there was no evidence of an association between GOS-E scores and anticoagulant use (OR = 0.71, 95% CI 0.48-1.05) or antiplatelets (OR = 1.02, 95% CI 0.73-1.42).

The authors concluded that while there was evidence of an effect of both anticoagulants and antiplatelets with in-hospital mortality after a major trauma, there was no evidence of an association between function and anticoagulant use after six months.

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Three clinical symptoms in ED patients with atraumatic back pain associated with cauda equine compression

Three key clinical findings have been found to be independently associated with an MRIconfirmed diagnosis of cauda equine compression.

Atraumatic back pain (i.e., with minimal tissue damage) is a common problem at emergency departments (ED), with a 2017 systematic review finding that it accounts for between 0.9% and 17.1% of all attendances.1 Cauda equine syndrome (CES) is a rare condition in which the lumbosacral nerve roots are compressed (hence the term cauda equine compression) that is commonly due to a central disc prolapse at the L4/5 or L5/SI level.² There is some uncertainty over the incidence of the condition but a 2020 systematic review found a combined estimate of 0.27% from four studies of those with low-back pain presenting to secondary care.³ Untreated or missed as a diagnosis, CES can lead to permanent neurological dysfunction and which includes loss of bladder control, sexual function and a sensory/motor deficit. Although the diagnosis can be confirmed by MRI, access to this imaging modality is limited in ED hence clinicians need to identify those patients who require urgent imaging.

Which, if any, clinical symptoms obtained during a routine examination have predictive accuracy for the diagnosis of CES, was the subject of a study by a team from the Department of Spinal Surgery, Salford Royal NHS Foundation Trust, Salford, UK.⁴ The team undertook a retrospective case review over a 4-year period of all ED atraumatic pain at a single site major trauma spinal referral centre. They included patients 18 years and older who had undergone a reference standard imaging (MR spine) due to a clinical suspicion of CES. The team undertook a univariate logistic regression analysis to identify those subjective and objective risk factors associated with a diagnosis of CES and included only those that were deemed statistically significant (p < 0.05) in a multivariate analysis.

Findings

During the 4-year study period, 2036 patients presented at the ED with back pain of which 996 were referred to exclude CES. These patients had a median age of 46 years and radiological compression of the cauda equine was reported in 11.1% (111/996) of them, of whom 109 went on to have urgent surgical decompression. Looking at the clinical symptoms, both bilateral leg pain (with or without back pain) was significantly more frequent in those with CES (p < 0.001) as was the perception of bilateral weakness (p = 0.002).

In multivariate analysis, there were three significant and independent predictors of CES. Bilateral leg pain, with or without back pain (odds ratio, OR = 1.90, 95% Cl 1.2–3.0, p = 0.006), objective sensory loss in a dermatomal distribution (OR = 1.70, 95% Cl 1.1–2.7, p = 0.01) and finally, the loss of bilateral ankle and/or knee jerk reflexes (OR = 3.4, 95% Cl 1.8–6.6, p < 0.0001). The team found limited diagnostic utility for a digital rectal examination.

The authors concluded that further prospective work was needed to validate their findings and to develop risk prediction tools to guide emergency imaging decisions.



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Guideline-based acute paediatric asthma care infrequent in US emergency departments

An analysis of over 7 million ED visits for acute asthma in children has revealed how only 34% of visits were guideline adherent although this increased to 42% in paediatric ED centres.

According to the World Health Organization, asthma affected around 262 million people in 2019, leading to an estimated 461,000 deaths and is the most common chronic disease among children.1 Moreover, one US study found that visits to the emergency department (ED) for asthma in children increased by 13.3% between 2001 and 2010.² Guidance on the treatment of acute asthma within the FD has discouraged the routine use of chest X-rays and antibiotics while encouraging the use of systemic corticosteroids.³ Though some studies have examined the level of agreement with these individual recommendations, finding, for example, that the use of chest X-rays and antibiotics were less likely,4 no studies have examined these three quality markers, i.e., no chest X-ray, no antibiotics given and provision of systemic corticosteroids, simultaneously. Consequently, a team from the Division of Emergency Medicine, Boston Children's Hospital, Harvard Medical School, Boston, US, set out to examine the rates of adherence to these three indices during ED visits for children with asthma.⁵ For comparative purposes, the team also compared alignment with these measures in both general and paediatric ED centres.

The team used a cross-sectional design and captured data from the National Hospital Ambulatory Medical Care Survey, which is a nationally representative survey of hospital ED visits, and which is conducted annually. The researchers focused on all ED visits for patients aged between 2 and 18 years of age from 2005 to 2013 with a diagnosis of asthma and documentation of bronchodilator administration at the ED. They used a composite outcome measure based on the three criteria of administration of a systemic corticosteroid either in the ED or via a prescription, no use or prescription of an antibiotic and no chest X-ray being used.

Findings

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The dataset included 7,794,163 eligible ED visits with 877,342 made to a paediatric ED. Overall, 44% of visits were for children aged 2–6 years (59% male). The majority of children were of

White (54%) or Black (41%) ethnicity with the remainder being Hispanic or Latino (27%) or other (5%). When comparing general and paediatric ED visits, there was no difference in the rates of corticosteroid use (63% vs 62%, paediatric vs general, p = 0.80) although rates of antibiotic prescribing were significantly lower at paediatric centres (11% vs 20%, paediatric vs general, p = 0.01). In contrast, use of chest X-rays was significantly higher in general EDs (26% vs 40% , paediatric vs general, p = 0.002).Overall, guideline-based acute asthma paediatric care was significantly more likely at a paediatric ED centre (42% vs 31%, paediatric vs general, p = 0.004). Interestingly, multivariate analysis revealed how only paediatric ED type, Black ethnicity and hospitals located in the western part of the country were independently associated with guideline-compliant care.

The authors concluded that guideline-based ED care for acute exacerbations of asthma occurred relatively infrequently in US EDs but was more common, although still less than optimal, within paediatric ED centres. They called for future studies to examine the factors associated with optimal, guideline-based care.



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Higher qSOFA scores predictive of mortality among ED trauma patients

Among trauma patients in the emergency department (ED), the quick sequential Organ Failure Assessment score (qSOFA) has shown good predictive value for mortality.

Road traffic accidents are often fatal with data from 2015 compiled by the World Health Organization showing that every year the global number of fatal road traffic accidents is around 1.25 million.¹ While several tools such as the Revised Trauma Score² (RTS) and the Trauma and Injury Severity Score³ have been developed to rate both the severity of a trauma and as a prognostic guide, these scores require calculation via formulas that are too complicated for use in the emergency department (ED) resuscitation room. One potential tool is the qSOFA and this has been used to predict mortality risk in patients both with⁴ and without infection.⁵

How well the qSOFA score might perform in predicting mortality in ED resuscitation rooms is yet to be determined and was the subject of a retrospective study by a team from the Department of Critical Care Medicine, the First Affiliated Hospital of Soochow University, Jiangsu Province, China.⁶ The qSOFA score ranges from 0 to 3 and has three components: a systolic blood pressure (SBP) of 100mmHg or less, a respiratory rate (RR) of 22/min or greater and altered mentation. Over a three-year period, the team divided patients into two groups: survivors and non-survivors and then four subgroups according to their qSOFA score. They also used the Glasgow Coma Score (GCS) and used this to calculate the RTS score, which is the sum of the GCS, SBP and RR. The main study endpoint was mortality in the ED

resuscitation room and multivariate regression was used to determine the association between qSOFA scores and mortality. In addition, receiver operating characteristic (ROC) curve analysis was used to assess the mortality predictive ability of qSOFA scores.

Findings

A total of 1739 patients were included in the analysis, 1695 survivors with a mean age of 51 years (73% male) and 44 non-survivors (mean age 50 years, 77.3% male). In terms of the qSOFA scores, 57.8% had a score of 0, 33.3% scored 1, 8.1% scored 2 and 0.75% scored 3. In addition, the proportion of patients dying increased significantly with qSOFA scores, e.g., 0.60%, 3.38%, 12.06% and 15.38% for qSOFA scores of 0, 1, 2 and 3, respectively (p < 0.001). There was also a significant difference in the mean time spent in the ED (4 vs 13 hrs, survivors vs non-survivors, p < 0.001).

Mortality was significantly associated with qSOFA scores with qSOFA scores of at least two were associated with a significant increased risk of death. For example, using a qSOFA score as the reference point, a qSOFA score of 2 was associated with a nearly seven-fold increased risk of death (odds ratio, OR = 6.80, 95% Cl 1.79-25.90, p = 0.005) and a qSOFA score of 3 with a 24-fold increased risk (OR = 24.42). Using the area under the receiver operating curve (AUC), qSOFA scores had a predictive value for mortality of 0.78 (95% Cl 0.72-0.85).

Concluding, the authors stated that the qSOFA score can be used to assess the severity of ED trauma patients and has a good predictive value for mortality.



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Significant increase in ED visits for bike-related injuries during the pandemic

Researchers have identified ED visits for bike-related injuries increased during the pandemic although these were soft-tissuerelated but no more serious than in previous vears

An increased popularity of bike riding in Canada in 1990 led to a 60% increase in the number of emergency department (ED) visits that were attributable to carelessness or poor bike control.¹ Five years later, a report by the US, the Centers for Disease Control and Prevention, noted how nearly 1000 people die from injuries caused by bicycle crashes and that 550,000 people are treated in an ED for bike-related injuries.² Despite the propensity for accidents, the COVID-19 pandemic led to a boom in sales of bicycles, with a report from the Bicycle Association in the UK noting that between April and June 2020, bicycle sales increased by 63% year-on-year.3

But whether increased sales led to a higher incidence of accidents among children during the pandemic is uncertain and this was the question posed by a team from the Department of Pediatric Emergency Medicine, The Hospital for Sick Children, Toronto, Canada.⁴ They conducted a cross-sectional study of ED visits to their children's hospital between March and October 2020 and compared the level of visits with the same time period for two previous vears: 2018 and 2019.

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The researchers included all patients younger than 18 years of age and who presented at the ED with a bicycle-related injury from pedal bicycles, bicycle trailers and E-Bikes. However, they excluded cases where a pedestrian was injured and motorised bicycle-related injuries (e.g., dirt bikes). Data collected from hospital injury records included demographics, chief complaint, triage acuity at presentation and the use of helmets. Acuity was assessed using the Canadian Emergency Department Triage and Acuity Scale (CTAS), which ranges from 1 (critical) to 5 (non-urgent). Outcomes were classed as "admission to hospital", "left without being seen" or "discharged home from the ED". Among those admitted, the researchers further categorised patients as admitted to the floor, requiring immediate surgery or admission to the intensive care unit.

Findings

In terms of the number of visits, there were 1215



bike-related visits during the study period; 234 in 2018, 305 in 2019 and 676 in 2020. The mean age of all children was 9.5 years (67% male) and the median CTAS score was 3. The most common injury was a fracture (38.8%) and while this was numerically higher during the COVID-19 period (41.9% vs 37.5%, COVID vs pre-COVID), the difference was not statistically significant but there were significantly more bike injuries per month during the COVID-19 period compared to other times (p = 0.041). A comparison of pre-COVID-19 and COVID-19 time periods also revealed how there was a higher incidence of soft tissue bike-related injuries (28.4% vs 38.6%, p < 0.001). In contrast, there was a lower incidence of lacerations (24.3% vs 19.2%, pre vs COVID-19, p = 0.03) and multi-trauma injuries (4.3% vs 1.3%, pre vs COVID-19, p = 0.001). However, there were no significant differences for severe injuries or any other injury category.

Despite the increased rates of injury, the authors maintained that the benefits of cycling outweighed the risks and concluded that bike-related injuries increased during the pandemic and while soft tissue injuries were the most common reason, there was no difference in severe injuries compared to previous years.

NICE updates guidance on the use of casirivimab and imdevimab in COVID-19



The National Institute for Health and Care Excellence (NICE) has made revisions to its original COVID-19 rapid guideline: managing COVID-19 (NG191) that was originally produced in March 2021 to take account of emerging evidence on the effectiveness of different therapies and, in particular, patients who are hospitalised with the virus.

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Casirivimab and imdevimab is a neutralising monoclonal antibody combination that binds to two different sites on the COVID-19 spike protein and in doing so, prevents entry of the virus into host cells, thus inhibiting viral replication. The evidence for Ronapreve and which was used by NICE to make its latest recommendations, came from data in the RECOVERY trial undertaken by researchers at Oxford University and the results of the trial are available as a preprint.² The study enrolled 9,785 patients hospitalised with COVID-19 and who were randomised 1:1 to a single dose of intravenous casirivimab (4g) and imdevimab (4g) (n=4839) and compared with a group assigned to usual care (n=4,946). Since the trial recruited patients across 127 hospital sites throughout the UK, the definition of usual care varied but included corticosteroids (94%), aspirin (28%), remdesivir (25%), colchicine (23%) and tocilizumab or sarilumab (16%). For the trial, the mean age of participants was 61.9 years (63% male) and 54% were seropositive at the point of randomisation. The primary outcome was 28-day all-cause mortality.

Study outcomes

In terms of the primary outcome, overall mortality was not significantly different between those assigned Ronapreve or usual care (relative risk, RR = 0.94, 95% CI 0.87-1.02) and with seropositive individuals (RR = 1.07, 95% CI 0.94-1.22). However, for seronegative patients, there was a significant mortality benefit (RR = 0.82, 95% CI 0.73-0.92). In addition, there was a reduction in the number of seronegative patients progressing to invasive mechanical ventilation and the median duration of hospital stay was reduced from 17 days (usual care) to 13 days.

Based on the evidence from this single trial, the NICE panel agreed to recommend casirivimab and imdevimab to hospitalised seronegative COVID-19 patients aged 12 and over. A recognised limitation of the RECOVERY trial noted by NICE was that there was a lack of data on different doses of casirivimab and imdevimab, among immunocompromised patients and those who had been vaccinated. An additional problem was that safety outcomes were not collected throughout the study and NICE concluded that the safety profile of the combination is yet to be determined. Despite these limitations, the panel agreed that Ronapreve should be used for all eligible patients.

Positive CT-PA and haemoptysis associated with meeting 4-hour target in ED for PE patients

Within an emergency department (ED), researchers identified that a positive computed tomography pulmonary angiography (CT-PA) and haemoptysis were the only factors associated with meeting the 4-hour target in an ED.

A venous thromboembolism, which includes both deep vein thrombosis and pulmonary embolism (PE), is the third most common cardiovascular disease with an overall incidence of 100-200 per 100,000 people.¹ Moreover, a PE is potentially life-threatening and because the condition lacks a specific set of symptoms, the diagnosis has become heavily reliant on non-invasive imaging. In fact, CT-PA is now recognised as the gold standard for the diagnosis of a PE.² Left untreated an acute PE has a mortality rate of up to 30% and potentially up to two-thirds of patients with a PE can die within 2 hours of presentation.³ Thus, a prompt diagnosis can have a significant impact on mortality and in fact, some evidence suggests that longer waiting times with an emergency department (ED) are associated with a greater risk in the short-term, of death and admission to hospital.⁴ The introduction of a 4-hour

The introduction of a 4-hour target in ED therefore seeks to reduce the time patients spend in the department.

However, the need for a CT-PA scan might increase the overall time spent within the ED and therefore breach the 4-hour target. Although clinical care should not be driven solely by the need to achieve a time-based target, a team from the Department of Radiology, Salmaniya Medical

Complex, Bahrain, Saudi Arabia, wondered if there were specific patient or environmental factors which might influence the duration of stay in the ED. They undertook a retrospective analysis focussing on patients presenting with a suspected PE and for whom a CT-PA scan was performed.⁵ The team sought to identify which, if any, patient or environmental factors were associated with meeting the hospital's 4-hour target. They collected patient demographic and clinical data as well as the time of presentation and deposition, calculating the length of stay in ED as the difference between these two times. Multivariate logistic regression analysis was used to determine independent factors associated with meeting the 4-hour target.

Findings

A total of 232 patients (32.8% male) of whom 80.2% were under 50 years of age, presented at the ED and underwent a CT-PA scan to rule out a PE. Overall, only 14.6% had a PE and a D-dimer assay had been requested for 59.1% of them. The overall median time to deposition from the ED was 5.2 hours and the only clinical factors that were significantly associated a lower time to disposition were the presence of hypoxia (p = 0.04) and an altered level of consciousness (p = 0.01). The time to deposition was longer among those who had a D-dimer test but this difference was not significant (p = 0.43). Overall, patients found to have a PE in the CT-PA scan also had a significantly shorter duration of stay in the ED (p = 0.02). Another factor which influenced the duration of stay was the day on which patients were seen, with those who attended at the weekend having

a shorter length of stay (p = 0.01). In the multivariate regression analysis, only two factors were independently associated with a stay of under four hours. The presence of a positive CT-PA scan (odds ratio, OR = 2.2, 95% CI 1.1-4.8, p = 0.02) and the haemoptysis (OR = 10.4, 95% CI 1.2-90.8, p = 0.03). Commenting on these findings, the authors noted that while guidelines suggest that a D-dimer test is performed

before a CT-PA scan, performing this test only added around 30 minutes to the overall time to deposition. They suggested that although their study had focused only on patients who had a CT-PA scan, clinicians should not be reluctant to request a D-dimer test simply to achieve the time-based target.

They concluded that meeting the 4-hour target was not significantly associated with most patient and environmental factors and that careful clinical assessment prior to a CT-PA scan was needed because a negative scan result may be associated with failure to meet the time-based target.

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Simulation-based training improves retention of paediatric resuscitation skills

After initial paediatric resuscitation training, skills can decay as early as 4 months later. Inclusion of simulation-based training 4 months after the initial training appears to improve retention scores when re-assessed after 8 months.

After completion of the American Heart Association Pediatric Advanced Life Support (PALS) programme, it is recommended that recertification should occur every 2 years.¹ Despite this recommendation, a systematic review of studies examining retention of adult advanced life support knowledge and skills, found that both knowledge and skills decay 6 months to 1 year after training.² Furthermore, the incidence of in-hospital cardiopulmonary arrests in paediatric patients is very low, ranging from 0.7% to 3% of all hospital admissions.³ Consequently, the capacity to master these skills through experience in clinical practice is limited. One approach to ensure that the necessary medical knowledge and skills are achieved is through a simulated-based curriculum, and this has been shown to enhance skills for handling medical emergencies.4

However, while this approach improves knowledge, it is less clear whether the technique supports the retention of knowledge.

This led a team from the Department of Pediatrics, University of Chicago, US, to explore the impact on retention of resuscitation skills. 8 months after a PALS course when reinforced by an adjunct simulation-based curriculum, 4 months after the initial PALS course.⁵ The team undertook a randomised, partially double-blind, controlled trial with first-year paediatric residents, who were blinded to the purpose of the study. To evaluate PALS procedural and cognitive skills, the residents had to complete simulation-based assessments (SBAs) on chest compression, airway management with bagvalve mask ventilation, intraosseous access and code team leadership. For each of the SBAs, a knowledge assessment tool was developed and used by trained raters, who watched video recordings of each resident performing the SBAs. The intervention group participated in SBAs and the simulation-based curriculum at 4 and 8 months after the PALS training, whereas the control group did not undergo the 4-month training session. The primary outcome was the changes in retention skills score at 8 months after the PALS course and assessed by the same raters at each time point.

Findings

A total of 24 residents were included and equally matched between the intervention and control groups. After 8 months, the overall mean per cent score for the intervention group on all four SBAs was 0.57 (95% CI 0.55-0.59) and 0.52 (95% CI 0.50-0.54) for the control group and this difference was statistically significant (p = 0.037). However, there was no significant difference between the two groups for each of the four individual SBAs. In addition, the intervention group had greater retention of cognitive knowledge mean scores (0.78 vs 0.68, intervention vs control, p = 0.049). The overall SBAs mean scores for all residents reduced from a mean percent of 0.61 at baseline to 0.55 at 8 months.

The authors commented on how the simulation-based curriculum significantly improved residents' paediatric resuscitation skills. They concluded that this approach provided a suitable pathway for safeguarding against the decay of resuscitation skills.

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Unintentional opioid exposure in young children a common problem at EDs

The majority of children with unintended opioid exposure attending an emergency care department were discharged without incident and even those admitted had favourable outcomes.

One study of US emergency department (ED) paediatric visits for poisoning from prescription opioids, identified 21,928 visits between 2006 and 2012.¹ Any cases of poisoning in children under 6 years are generally considered to be unintentional. In a further analysis of unsupervised paediatric medication exposures at emergency departments, prescription opioids were the most common class of medicines involved.² While there are several publications examining the prevalence of unintentional paediatric opioid exposure, much less attention has been paid to the outcomes associated with these ingestions.

This prompted a team from the Department of Pediatric Emergency Medicine, University of Alabama, US to undertake a retrospective analysis of the data collected by the Regional Poison Control Centre (RPCC), in Alabama, of children aged 0 to 6 years with possible opiate exposure over a three period.³ Using the RPCC database, the team identified cases for all of the major opioid drugs including buprenorphine, codeine, fentanyl, hydrocodone, hydromorphone, methadone and oxycodone. Additional information collected included basic demographics, clinical data, including symptoms and the outcomes if the child was admitted.

Findings

A total of 429 charts were identified as meeting the inclusion criteria. The median age of children was 2 years (64% male). Caretakers reported symptoms in 140 (32%) of all cases referred to the ED although the remaining 289 were asymptomatic. There were 113 children referred to the ED by the RPCC service and 122 who presented directly to the department. Therefore 235 were seen at the ED. of which in 152 cases (66%) there was no medical intervention. From a total of 231 opioid exposures, the most common drug was buprenorphine (13%), followed by codeine (8.6%). There were 65 children (28%) who were admitted to hospital, 41 directly from the ED and 24 from an outside facility. Among those admitted, the majority, 28, were 1-year olds. Furthermore, 5 of these children were admitted to intensive care and 28 of the children received naloxone, 3 required multiple doses and 5 a continuous infusion. There were no fatalities although one patient had ingested a significant amount of methadone and required active resuscitation and a naloxone drip. Overall, the median length of hospital stay was one day.

In their conclusion, the authors noted that although 28% of children had required admission to hospital, the outcome was positive for most with only a small number requiring medical intervention, mainly in the form of naloxone.

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