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Main Title:

Evaluation of pre-hospital COVID-19 rapid antigen tests by paramedics and their use in a direct admission pathway

Running Title:

Pre-Hospital COVID-19 rapid antigen tests

Authors:

Dr Alexander Richards[1], Dr Muhammad Muddassir[1], Dr Fiona Sampson[2] (r), Ms Laura MacLachlan[1], Ms Elisha Miller[3], Dr Joseph Fitchett[4], Dr Fiona Bell[3], Dr Monica Ivan[1], Dr Patrick Lillie[1,5], Dr Anda Samson[1], Dr Nicholas Easom[1, 5] (nicholas.easom@nhs.net)

1. Infection Research Group, Department of Infection, Hull University Teaching Hospitals NHS Trust, Hull, UK
2. School of Health and Related Research, University of Sheffield, Sheffield, UK
3. Yorkshire Ambulance Service NHS Trust, Wakefield, UK
4. Institut Pasteur de Dakar, Dakar, Senegal
5. Hull York Medical School, University of Hull, Hull, UK

Corresponding Author:

Dr Nicholas Easom

Infection Research Group, Department of Infection, Hull University Teaching Hospitals NHS Trust, Hull, UK

Email Address: nicholas.easom@nhs.net

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We read with interest the article by Owen S.I. et al regarding evaluation of Lateral Flow Immunoassays to detect SARS-CoV-2 antibodies[1]. Lateral Flow Devices (LFD) have found widespread use in clinical diagnosis and asymptomatic testing. We present the first reported use of LFD for pre-hospital point of care COVID-19 respiratory antigen testing for the rapid diagnosis and triage of COVID-19.

COVID-19 first emerged in December 2019 following an outbreak in Wuhan, Hubei province, China[2], rapidly escalating to a global pandemic[2,3,4] resulting in unprecedented health care pressures. The first cases in the UK were diagnosed in January 2020[4]. By January 2021 over 25,000 patients with COVID-19 were being admitted to UK hospitals daily[5].

In the Hull and East Yorkshire region, ambulance crews had increased waiting times to handover patients to Accident and Emergency, and oxygen capacity in the main admitting

hospital was stretched to capacity. In response to these pressures, we established two complementary projects: PRACTICAL (Pre-hospital RApid COVID-19 Testing for Improved CAre in HulL) 1: A performance assessment of a lateral flow rapid antigen test for COVID-19 (COVIOS Ag Covid-19 rapid antigen test; legal manufacturer Mologic UK)[6] performed by ambulance paramedics attending to patients; and PRACTICAL 2: A direct admission pathway separate from Accident and Emergency for patients with a positive COVID-19 test within 14 days (including same-day LFD by paramedic).

PRACTICAL 1 was a single arm, observational, assay validation and acceptability study. Paramedics with Good Clinical Practice training were identified and trained for the study and use of the test. Methodology developed between Yorkshire Ambulance Service NHS Trust (YAS) and Hull University Teaching Hospitals NHS Trust (HUTH) with agreed inclusion and exclusion criteria.

Inclusion criteria included patients aged 18 and over that were likely to be admitted regardless of COVID symptoms with stable oxygenation status. Exclusion criteria included confusion, oxygen saturations <92% on oxygen, pregnancy and requirement to access an acute pathway (e.g. thrombolysis, trauma). Enrolled participants gave verbal consent and patients unable to give informed consent were not eligible.

Paramedics consented and conducted the LFD tests. The ambulance 'in-motion' status along with assay start and result time were recorded. Results of LFD were compared against first in-hospital PCR/NAAT test and discharge diagnosis or cause of death. Platforms used for routine COVID-19 testing were Cepheid COVID-19 PCR and Hologic Panther COVID-19 NAAT Assay. Sensitivity, specificity, positive and negative predictive values with 95% confidence intervals were calculated comparing the LFD results to laboratory confirmed PCR results and clinical diagnosis using Prism Statistical Software by GraphPad[7].

To complement LFD testing, a pathway of direct admission to a COVID-19 ward was established. PRACTICAL 2 was a service evaluation of referrals received by HUTH from YAS ambulance crews following a COVID-19 diagnosis either by LFD or community testing between 20th January (first patient admitted) and 5th March 2021.

Patients were considered appropriate for direct admission if age 18 or over with a positive COVID-19 test within the last 14 days. Due to staffing requirements patients were admitted 9am-4pm weekdays only. Exclusion criteria were as for PRACTICAL 1. Disease severity was assessed using National Early Warning Score 2 (NEWS2) and ISARIC 4C scores[8]. Transfer time, length of stay and outcome were recorded.

Both projects were approved as service evaluation by the Clinical Effectiveness and Audit Team at HUTH and by YAS Research and Development.

PRACTICAL 1: Pre-hospital LFD was performed in 50 patients, with 32 having COVID-19 PCR as part of the assessment on arrival into hospital. Compared with PCR, sensitivity was 77.8% and specificity was 100% (Table 1), in keeping with previously reported test performance[6].

Not all patients during this period had symptoms meeting the Public Health England (now UK Health Security Agency) case definition[9], however the LFD detected COVID-19 in patients regardless of their symptomology. Compared against discharge diagnosis of COVID-19, sensitivity was 81.82% and specificity was 97.30%.

In 8 cases LFDs were developed with the ambulance in motion, attached to the dashboard using a pressure sensitive, reusable, putty-like adhesive. Five of these patients had subsequent PCR, in all five the PCR and LFD results were in agreement.

LFD was read at a median of 10 minutes (1 to 30 minutes) in accordance with manufacturer's instructions, PCR results took a median of 9 hours (01.21hrs to 22.56hrs).

PRACTICAL 2: The direct admission pathway received 18 referrals from the Yorkshire Ambulance Service, 12 fulfilled the admission criteria and were admitted. The median age of the patients assessed was 57 years old (range 43-90), all patients survived to discharge, with median length of stay of 5 days (Table 2).

Most patients presented with 3 or more symptoms, the most common being shortness of breath. The median NEWS2 was 4 with a median expected ISARIC 4C mortality[7] of 9.75%. Four patients required pre-hospital oxygen in the ambulance. The median ambulance handover time was 1 minute with a maximum of 33 minutes. Despite favourable outcomes the direct admission pathway was closed in early March 2021 as COVID-19 admissions fell and the receiving area was returned to its usual ward function.

PRACTICAL 1 & 2 show that the Ambulance paramedic-administered, pre-hospital LFD results compare favourably with PCR and clinical diagnosis, in keeping with reported test performance in laboratory and other clinical settings. A direct admission pathway with agreed criteria is safe and may offer benefits both in terms of efficient patient handover and potential infection control benefits by allowing cohorting of infectious patients from the moment of admission.

Lateral flow rapid antigen tests performed by paramedics during periods of high incidence have potential to streamline admissions for the benefit of health services and patients. This approach may have value as part of a "living with COVID" strategy and could be adapted to incorporate future combined influenza/COVID-19 LFDs[10].

Table 1

	Value	95% Confidence
LFD performance against PCR		
Sensitivity	78%	40% to 97%
Specificity	100%	85% to 100%
Positive Predictive Value	100%	-
Negative Predictive Value	92%	77% to 98%
LFD performance against Clinical Diagnosis		
Sensitivity	82%	48% to 98%
Specificity	97%	86% to 100%
Positive Predictive Value	90%	56% to 98%
Negative Predictive Value	95%	84% to 98%
LFD Result time (range)	10 minutes (1-30 minutes)	-
Median PCR/NAAT Result Time (range)	9 hours (01.21hrs to 22.56hrs	-

Performance of Lateral Flow Assay. PCR, polymerase chain reaction; NAAT, nucleic acid amplification test.

Table 2

Parameter	Value
Female	5/12 (42%)
Age (years)	57 (43-90)
Length of stay (days)	5 (0-12)
NEWS2 at admission	4 (0-8)
ISARIC 4C at admission	6.5 (3-14)
CRP on admission	107 (27-200)
Ambulance handover time (mins)	1 (0-31)

Patient demographics and clinical features. Values presented as median and range except for Female presented as fraction of total and percentage. NEWS2, National Early Warning Score 2; ISARIC 4C, International Severe Acute Respiratory and emerging Infection Consortium Coronavirus Clinical Characterisation Consortium; CRP, C-reactive protein.

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Conflicts of Interest

Dr Joseph Fitchett was previously employed by Mologic LTD from 2018 to 2021.

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