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A need for consensus on mortality reporting related to the coronavirus disease-2019 pandemic in ongoing and future vascular registries and trials.



As the severe acute respiratory syndrome coronavirus-2 continues to take more lives, quite a few of these will be from the vascular population,¹⁻³ typically older and with multiple comorbidities, recognised risk factors for coronavirus disease (COVID)-19–related mortality.⁴ Some such patients will be involved in ongoing vascular trials and registries.

Presenting an “overall mortality rate” is obligatory at registry/trial reporting, particularly specifying the cause of death (COD). There may be some “unknown COD,” but these should be a minority, particularly in robust prospective studies. Some unknown COD may be attributable to COVID-19, with many dying without COD confirmation. This is related to lack of testing, or high false negative rates, with controversy surrounding the accuracy of oropharyngeal vs nasopharyngeal swabs⁵ particularly for late testing.⁶

The issues arising from COVID-19-related deaths are two-fold: first, to do with accurate capture of COD (reporting issues), and second, the influence of increased deaths on the completeness of data in ongoing studies (outcome issues). This is a research concern,^{7,8} with calls to extend trial durations,⁹ and may necessitate post hoc/retrospective power calculations to reassess statistical validity of studies.

We therefore hypothesize four possible scenarios related to mortality reporting: (1) patients with accurate categorization of COVID-19-related COD; (2) patients with prior confirmed COVID-19 infection who recover but die later with unknown COD; (3) patients dying from an unknown cause during the pandemic, where COD is uncertain; and finally (4) accurate capture of non-COVID-19-related COD. Options 1 and 4 are qualitatively most desirable in terms of data capture.

Global clinical uncertainty¹⁰ has implications for registries that report on mortality. This concern pertains to both ongoing and to future study design, as we cannot predict patterns of disease chronicity or repetitiveness. This may lead to similar outcomes as indicated: (1) accurate COD capture, (2) inaccurate data capture leading to higher censoring at survival analysis, and (3) loss of patients in smaller studies due to high unexpected mortality, rendering them underpowered and redundant.

Some editorial consensus is needed to guide adequate mortality reporting, to avoid misguided assessments that may lead to misleading conclusions.

Andrés Reyes Valdivia, MD, PhD, FEBVS, FACS

Department of Vascular and Endovascular Surgery
Ramón y Cajals University Hospital
Madrid, Spain

Arindam Chaudhuri, MBBS, MS, FRCSEd, MSc, FRCS

Bedfordshire – Milton Keynes Vascular Centre
Bedford, United Kingdom

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A protocol for central venous access in patients with coronavirus disease 2019



From our single tertiary-center experience, many patients who develop coronavirus disease 2019 (COVID-19) infection require rapid escalation of care with mechanical ventilation, multiagent sedation and vasopressor support. Early on, more than 430 patients were hospitalized with approximately 25% requiring mechanical ventilation and intensive care unit care. These

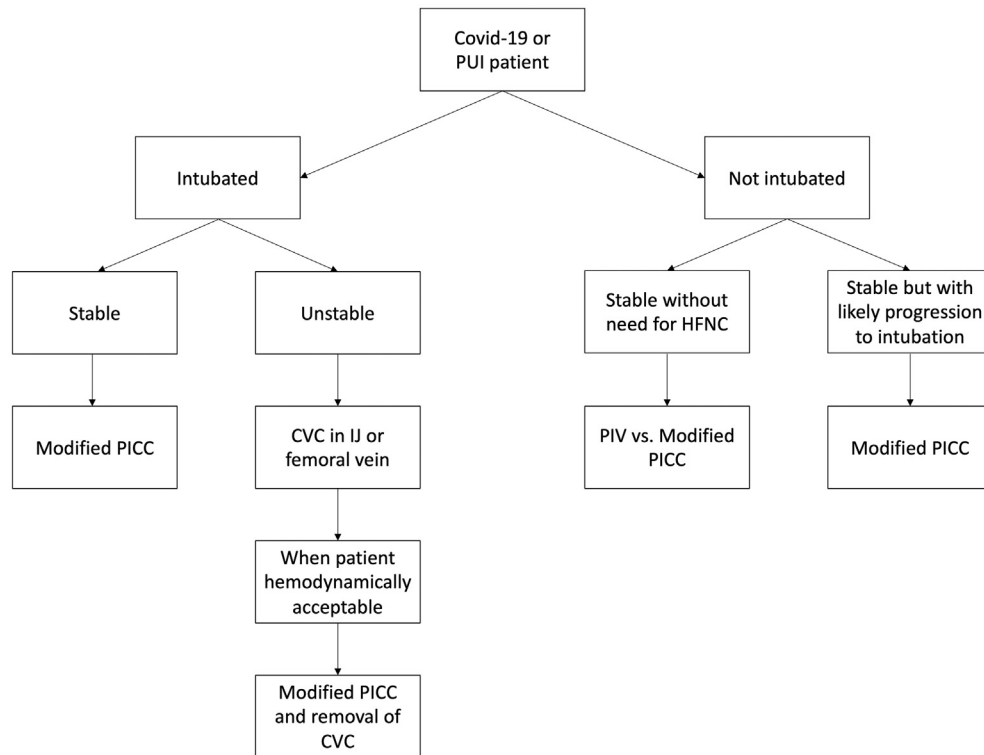


Fig. Guidance protocol for PICC insertion depending on the patient's clinical condition. *HFNC*, high-flow nasal cannula; *IJ*, internal jugular; *PUI*, person under investigation.

patients require central venous access catheters (CVC), hence increasing significantly the exposure time for both physicians and nurses. After discussion between intensive care unit physicians and the vascular surgery team, a decision was made to utilize triple-lumen peripherally inserted central catheters (PICC) as the preferred means of establishing central vein access. A protocol for modified PICC insertion (Fig) was designed to meet the high demand for access.

With ultrasound guidance, we identified a feasible upper arm superficial (cephalic or basilic) or deep (brachial) vein and inserted a PICC without the catheter-navigation and tip-confirmation technology. To avoid propagation of the catheter tip in the right atrium and subsequent need for catheter adjustment, we cut the length of the PICC at about the proximal one-third of the clavicle. This way, the procedure takes 15-20 minutes total time in the patient's room, the catheter tip is within the ipsilateral subclavian or brachiocephalic vein and a confirmation chest radiograph is not required before use.

During the first stages of the COVID-19 pandemic, a dedicated PICC-team performed 112 PICC insertions in 112 patients with COVID-19. The technical success was 100% and the basilic vein was most commonly used. Follow-up after PICC insertion ranges from 10 to 21 days. None of the patients developed catheter-related infections or upper extremity deep venous thrombosis related to PICC placement. One patient

developed limited-extend cephalic vein superficial thrombophlebitis while on therapeutic anticoagulation, so continuous use of the PICC was recommended. No line malfunction was reported, and no requests were received to replace PICC. Of note, an institutional anticoagulation protocol based on D-dimer levels was being followed for all coronavirus patients at the time.

Many patients with severe COVID-19 require pressor support early in the hospital course to maintain hemodynamic stability.¹ These patients require mechanical ventilation for a prolonged period.² The use of PICC as preferred CVC offers a number of advantages: (a) the time required for insertion, hence staff exposure is low; (b) PICCs can stay in place longer than CVCs, thus decreasing the need for line replacement; (c) the rate of complications requiring operative intervention with PICCs is lower than that seen with CVCs³; (d) although the infection rate of CVCs and PICCs appears to be similar in the literature, the median time to development of bloodstream infection with PICC is significantly longer⁴; and (e) given the high rates of acute renal failure, central access (internal jugular and femoral veins) remains available for placement of dialysis catheters.

These short-term observations support the strategy of using PICCs as low risk, effective, and reliable option for central venous access in patients with COVID-19. We intend to continue monitoring our patients and report their longer term outcomes.

Patrick T. Jasinski, MD
Georgios Tzavellas, MD

Division of Vascular and Endovascular Surgery
Department of Surgery
Stony Brook Medicine
Stony Brook, NY

Jerry A. Rubano, MD
Daniel N. Rutigliano, DO

Division of Trauma Surgery and Critical Care
Department of Surgery
Stony Brook Medicine
Stony Brook, NY

Edvard Skripochnik, MD
Apostolos K. Tassiopoulos, MD

Division of Vascular and Endovascular Surgery
Department of Surgery
Stony Brook Medicine
Stony Brook, NY

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Moving forward: Ensuring quality research in vascular surgery during COVID-19



In their article, Valdivia and Chaudhuri discuss the impact of deaths from the coronavirus disease 2019 (COVID-19) on the outcomes of trials and registries, importantly highlighting the negative impact on the accuracy of databases and calling for improved guidelines surrounding mortality reporting.¹ COVID-19 is a double-edged sword: whereas it has brought new research questions in times of uncertainty, it has equally complicated traditional academic pursuits. Although trials and registries should be considered in a case-by-case manner, timely interventions are needed to protect participants' safety first and foremost. Studies, where possible, should consider halting or delaying the recruitment of new patients, establishing on-site precaution measures, and maximizing follow-ups by telemedicine.^{2,3} Revision of statistical analyses, data interpretation,

and protocols is unavoidable as, similar to patient safety, integrity in research should remain prioritized.

This pandemic can, however, also become an opportunity to revisit how clinical research is conducted. Learning from current challenges in accounting for heightened mortality due to COVID-19, trials and registries need to be structured for unexpected events that would significantly influence the number of participants or their outcomes. Future pandemics and global crises are bound to occur, and devising prespecified protocols for patient follow-up, data storage, and human resource management will be crucial in ensuring the consistency of clinical research when resources are redirected toward emergency response.^{3,4} Furthermore, there is potential for a larger role for citizen-driven science and self-reported outcomes in advancing pandemic-related research and beyond, reducing the burden on clinical providers and scientists while still ensuring the advancement of our field.

One silver lining of the pandemic for research will be the vast body of literature that is being generated on disease-specific outcomes affected by COVID-19.⁵ New international collaboratives like the Vascular Surgery COVID-19 Collaborative (VASCC) and the COvid-19 Vascular sERvice (COVER) are actively collecting information on the consequences of surgery delays and COVID-19 infections in vascular patients.^{6,7} Only through cooperation, transparency, and solidarity between researchers will we be able to bounce back from the darkness of the COVID-19 era and build resiliency into surgical research to navigate future crises.

Xiya Ma, MD, MSc

Faculty of Medicine
Universite de Montreal
Montreal, Quebec, Canada

Jessica G. Y. Luc, MD

Division of Cardiovascular Surgery
Department of Surgery
University of British Columbia
Vancouver, British Columbia, Canada

Dominique Vervoort, MD

Johns Hopkins Bloomberg School of Public Health
Baltimore, Md

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