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Review article

The impact of COVID-19 pandemic on vascular registries and clinical trials

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ABSTRACT

Quality improvement programs and clinical trial research experienced disruption due to the coronavirus disease 2019 (COVID-19) pandemic. Vascular registries showed an immediate impact with significant declines in second-quarter vascular procedure volumes witnessed across Europe and the United States. To better understand the magnitude and impact of the pandemic, organizations and study groups sent grass roots surveys to vascular specialists for needs assessment. Several vascular registries responded quickly by insertion of COVID-19 variables into their data collection forms. More than 80% of clinical trials have been reported delayed or not started due to factors that included loss of enrollment from patient concerns or mandated institutional shutdowns, weighing the risk of trial participation on patient safety. Preliminary data of patients undergoing vascular surgery with active

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COVID-19 infection show inferior outcomes (morbidity) and increased mortality. Disease-specific vascular surgery study collaboratives about COVID-19 were created for the desire to study the disease in a more focused manner than possible through registry outcomes. This review describes the pandemic effect on multiple VASCUNET registries including Germany (GermanVasc), Sweden (SwedVasc), United Kingdom (UK National Vascular Registry), Australia and New Zealand (bi-national Australasian Vascular Audit), as well as the United States (Society for Vascular Surgery Vascular Quality Initiative). We will highlight the continued collaboration of VASCUNET with the Vascular Quality Initiative in the International Consortium of Vascular Registries as part of the Medical Device Epidemiology Network coordinated registry network. Vascular registries must remain flexible and responsive to new and future real-world problems affecting vascular patients.

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1. Introduction

After the global shutdown in March of 2020, quality improvement programs and clinical trial research experienced disruption due to the coronavirus disease 2019 (COVID-19) pandemic. Vascular registries showed an immediate impact with significant reductions in second-quarter vascular procedure volumes witnessed across Europe and the United States [1–3]. To better understand the magnitude and impact of the pandemic, organizations and study groups sent grass roots surveys to vascular specialists for needs assessment. Several vascular registries responded quickly by insertion of COVID-19 variables into their data collection forms. More than 80% of clinical trials have been reported delayed or not started due to factors that included loss of enrollment from patient concerns or mandated institutional shutdowns, weighing the risk of trial participation on patient safety [4–6]. Other reasons for clinical trial interruption included delayed ethical and regulatory approval of research projects and favored by a prioritization of COVID-19 research. Furthermore, the urgent need to redeploy staff to clinical areas resulted in directives to suspend data collection in National Clinical Audits [7].

This review highlights the pandemic's effect on multiple VASCUNET registries including Germany (GermanVasc), Sweden (SwedVasc), United Kingdom (UK National Vascular Registry [NVR]), Australia and New Zealand (bi-national Australasian Vascular Audit), as well as the United States (Society for Vascular Surgery Vascular Quality Initiative [VQI]). We will discuss changes made in registry data capture, highlighting concordance of variables and definitions across registries. A preliminary analysis of COVID-19–related data from the NVR provides an early assessment of outcomes. Registry variables related to COVID-19 emphasize the need for flexibility with ongoing challenges using real-world data in real time. Collaboration efforts by coordinated registry networks between VASCUNET and VQI and their integration with the International Consortium of Vascular Registries (ICVR) will be addressed.

The pandemic has also spurred rapid development of prospective patient cohort analyses, calling to attention research efforts by the Vascular and Endovascular Research Network (VERN) and the Vascular Surgery COVID-19 Collaborative (VASCC) and the challenges in "big data." In addition, barriers to registry modifications and continued clinical trial research in the midst of a pandemic will be reviewed.

2. Pathogenesis

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) responsible for the new coronavirus disease, COVID-19, infection demonstrates increased affinity for human angiotensin-converting enzyme 2 receptors in respiratory epithelium through spike protein modifications, increasing transmissibility during a previous SARS-CoV outbreak in 2002 [8]. Viral-induced activation of coagulation pathways and cytokine damage to vascular endothelium secondary to COVID-19 infection provoke a prothrombotic state affecting both microvascular and macrovascular arterial and venous systems [9]. Occult strokes, venous thromboses, pulmonary thromboembolism, Kawasaki-like syndrome in children and COVID toes are just some of the presentations seen from the novel coronavirus [10–12].

3. Vascular management decisions of COVID-19 infection

The global pandemic caused by SAR-CoV-2 forced the vascular community to re-assess the management of elective vascular disease and learn how to treat the vascular complications of COVID-19 infection. In the absence of published literature or evidence-based data about COVID-19, vascular surgeons had to assess the risk benefit of both routine and emergency care and evaluate each in the context of local community infection rates and available hospital resources. Rapidly developed guidelines from the American College of Surgeons (tiers 1 to 3) and the Vascular Activity Condition (VASCCON) became a useful aid for decision-making triage, as seen in Table 1 [13,14].

The implications of delaying treatment for routine vascular care and the rate of progression of disease are often not well defined, although the consequences are. Delays in treatment are variable for an asymptomatic carotid stenosis versus an asymptomatic > 6.5 cm abdominal aortic aneurysm (AAA) or a patient with an infected dialysis catheter in need of angioaccess [15].

Vascular registries are primarily procedural-based and not designed to evaluate delayed care or medical management. VQI recently released a Medical Management registry to collect data on medically managed patients with AAA, carotid stenosis, and lower extremity occlusive disease, but has

Table 1 – Types of surgical activities and levels of surgical activity condition and vascular surgery activity condition.

SURGCON level	Type of surgical activity	VASCCON
5	Evidence-based surgical practice	Clinical practice guideline directed care of AAA, CAS, PAD
4	Limitations on nonemergency surgery	Booked cases limited to AAA >6 cm, symptomatic CAS, CLTI
3	Severe limitations on nonemergency surgery	Booked cases limited to AAA >8 cm, symptomatic CAS, severe CLTI
2	Emergency surgery only	No booked cases, emergency cases include ruptured AAA, acute limb ischemia
1	No surgical activity	No emergency or booked surgery (patients with ruptured AAA are palliated)

From Forbes TL. Vascular surgery activity condition is a common language for uncommon times. J Vasc Surg 2020;72:391–2 [14], adapted with permission.
Abbreviations: AAA, abdominal aortic aneurysm; CAS, carotid artery stenosis; CLTI, chronic limb-threatening ischemia; PAD, peripheral artery disease; SURGCON, surgical activity condition; VASCCON, vascular surgery activity condition.

limited enrollment. Procedural registries can analyze the impact of comorbidities if the pertinent variables are in the collection form. New and unique variables must be added to the registries in order to provide data for analysis of new conditions.

The earliest insight into changes in practice patterns comes from surveys conducted with vascular surgeons [16]. A survey by Aziz et al [17] with US vascular surgeons showed that most noticed a decrease in clinic referrals, emergency department consults, and overall case volumes. Similarly, a survey by the COVER (COVID-19 Vascular Service) Study Collaborative showed that globally, there was a trend in the reduction in all peripheral vascular surgery, including carotid, aortic, and lower extremity arterial operations [18]. These surveys also indicate that many patients with vascular disease delayed seeking medical attention and experienced adverse consequences. News media outlets reported that a number of patients with heart attack and stroke avoided emergency departments or appropriate medical care, presenting late or dying at home [19].

Similar suppositions can be made for patients with AAAs, carotid artery stenosis, and severe peripheral arterial disease [20].

A review of current literature showed that COVID-19 infection is associated with an acquired hypercoagulable state. Nypaver et al [21] reviewed seven patients with COVID-19 who presented with stroke and concluded that COVID-19 is associated with increased thrombus formation in extracranial carotid arteries. Ilonzo et al [22] described thrombotic complications of 21 patients who were severely ill during the height of the pandemic in New York City. Overall mortality was 28.6% with more than three-fourths presenting with acute arterial thrombosis and critical ischemia. Increased mortality in patients with COVID-19 complicated by venous thromboembolism has also been reported [23].

Patients with COVID-19 can have a myriad of presentations in vascular beds, and registry databases will have to be flexible to respond rapidly to a changing clinical environment. There are important unresolved questions, such as when elective operations can be safely performed during a COVID-19 surge, which "elective" operations, for example, >6.5-cm AAA should be prioritized in the presence of restricted resources, and how long does the prothrombotic condition last after COVID-19 infection before it is safe to proceed with elective operations, such as treatment for claudication or varicose veins. Broadening the scope of databases to include new variables in a timely fashion will have the potential to address these important clinical dilemmas. Registry data may provide better understanding should another pandemic occur in the future.

4. Registry additions of COVID-19 variables

Determining the magnitude of the novel coronavirus infection on vascular disease management requires collecting new preoperative and postoperative clinical variables. Shortly after the onset of the pandemic, VQI (regional) and VERN (international) surveyed their membership. It was evident early on that many COVID-19 risk factors are also highly prevalent in vascular surgical patients, including advanced age, male sex, smoking, obesity, coronary artery disease, hypertension, chronic pulmonary disease, chronic renal disease, diabetes, and malignancy. Given the lack of knowledge about COVID-19, many vascular registries independently responded with rapid insertion of COVID-19–related variables into their data collection forms for monitoring impact. Multicenter study collaboratives were formed to better understand COVID-19's impact on patients with vascular disease (VASCC and COVER). The additional COVID-19–related variables are listed in Table 2. As these variables were developed independently, there were some minor differences noted across registries. COVID-19 infection status, procedure delays, disease worsening, and mortality were the most commonly chosen data fields. Timing of COVID-19 variable insertion into registry databases occurred as quickly as mid-April 2020 (UK NVR, SwedVasc) to early September 2020 (VQI). The speed of registry revision was remarkable, given additional variable insertion typically takes a minimum of 12 to 18 months. The NVR COVID-19 data fields were initially added to the peripheral artery disease and AAA datasets and went live in April 2020, and new variables were added to the carotid data set in June 2020 [24].

The addition of COVID-19 data fields was variable in other VASCUNET registries. The GermanVasc registry retrospectively surveyed COVID-19–related variables on a voluntary basis at participating centers. The Australasian Vascular Audit has not yet elected to collect COVID-19 data. Of note,

Table 2 – COVID-19–related variables per registry/study collaborative.

Variable	SwedVasc[a]	US VQI[b]	UK NVR[c]	COVER[d]	VASCC[e]
Registry origin	1987	2011	2005	NA	NA
COVID insertion date	April 2020	September 2020	April 2020	April 2020	April 2020
At procedure					
Exposure history	+	+	+	+	+
Test result at procedure	+	+	+	+	+
Symptom status	–	+	+	+	+
Procedure delay	+	+	+	+	+
Disease worsening	–	+	+	–	–
Adverse events					
Procedure change	–	–	+	+	+
Conversion	–	–	+	+	+
COVID reoperation	–	–	–	+	+
COVID graft occlusion	–	–	–	+	+
COVID DVT/VTE	–	–	–	+	+
COVID mortality at follow-up	+	–	–	+	+
COVID pneumonia	–	–	+	+	+
COVID status	+	+	–	+	+
Re-admission	–	–	–	+	+
Vaccination	–	–	–	–	–
Adverse events	+	–	–	+	+

Abbreviations: COVER, COVID-19 Vascular Service; COVID-19, coronavirus disease 2019; DVT, deep venous thrombosis; NVR, National Vascular Registry; VASCC, Vascular Surgery COVID-19 Collaborative; VTE, venous thromboembolism; VQI, Vascular Quality Initiative.

[a] SwedVasc captures procedure data for carotid, abdominal aortic aneurysm (AAA), peripheral artery disease (PAD)-peripheral vascular intervention (PVI), venous, and trauma. Follow-up is at 30 days and 1 year. Lifelong surveillance possible via national identifier.

[b] US VQI captures procedure data for 14 registries: carotid endarterectomy (CEA), carotid artery stenting (CAS), thoracic endovascular aneurysm repair (TEVAR)/complex endovascular aneurysm repair, endovascular aneurysm repair, supra- and infrainguinal bypass, open aortic, lower extremity bypass, PVI, amputation, inferior vena cava filter, varicose vein, venous stent, and hemodialysis. Follow-up is at 30 days and 1 year (9 to 21 months).

[c] UK NVR captures data for AAA, CEA, PVI, lower extremity bypass, and amputation. Follow-up is at 30 days.

[d] COVER is an international multicenter study collaborative project collecting outcomes of all major vascular surgery and procedures during COVID pandemic at 30 days, 6 months, and 12 months. It is led by the Vascular and Endovascular Research Network collaborative and sponsored by the University Hospital of Coventry and Warwickshire.

[e] VASCC is an international survey collaborative capturing procedure data on aortic, carotid, peripheral, venous, and hemodialysis focusing on procedure delay and COVID impact. No follow-up is recorded.

no registry or study collaborative is currently capturing data on vaccination status. This apparent oversight reflects more on the speed with which variable insertion and study collaboratives were developed before widespread vaccination and the burdensome nature of registry modification.

In addition, in April of 2020, the World Health Organization and Family of International Classification issued how a confirmed SARS-CoV-2 infection must be coded to generate reliable administrative data in the future. This has since received periodic updates as COVID-19 information has progressed [25].

5. Registry volumes

As mentioned previously, most registries experienced significant initial procedural volume decline at the beginning of the pandemic in March 2020. Similar to VQI reporting, initial UK NVR analysis confirmed declines in major vascular procedures in AAA (12%), carotid endarterectomy (38%), and lower limb bypass (38%) during April of 2020 [26]. By July 2020, elective volumes of AAA and CEA had returned to approximately 80% of prepandemic levels (Fig. 1). Table 3 demonstrates year-end recovery of 2020 procedure volumes to approximately 85% of 2018 and 2019. This value may be a slight underestimate, as some registries could not provide complete year-end totals. Notably, Sweden (which avoided formal shutdown of the society as part of its COVID-19 response) and Australia/New Zealand (where COVID-19 rates remained exceptionally lower than other countries) are two exceptions where restrictive measures were not placed on medical practice. When compared to 2019 values, carotid, aortic, and peripheral arterial procedures (range, 84% to 104%) were impacted less than varicose vein, inferior vena cava filter and venous stenting (range, 66% to 85%). We were unable to determine whether COVID-19 caused a notable shift to more endovascular approaches over open procedures at this high-level analysis, as survey reports suggest. Individual-center reports indicate an endovascular-first approach likely reflects competing interests on surge capacity for intensive care unit resources from other services and risk of staff exposure to the virus [27]. Ongoing assessment will be necessary to determine whether this perception is real. Interestingly, in Germany (which implemented extensive restrictions of public life and health services in March of 2020), a decline of registry volumes and emergent admissions in administrative registries was observed, and no change in management was apparent. Elective (asymptomatic) to nonelective (symptomatic or emergent) volume ratios for aortic and infrainguinal bypass in 2020 declined from those in 2018

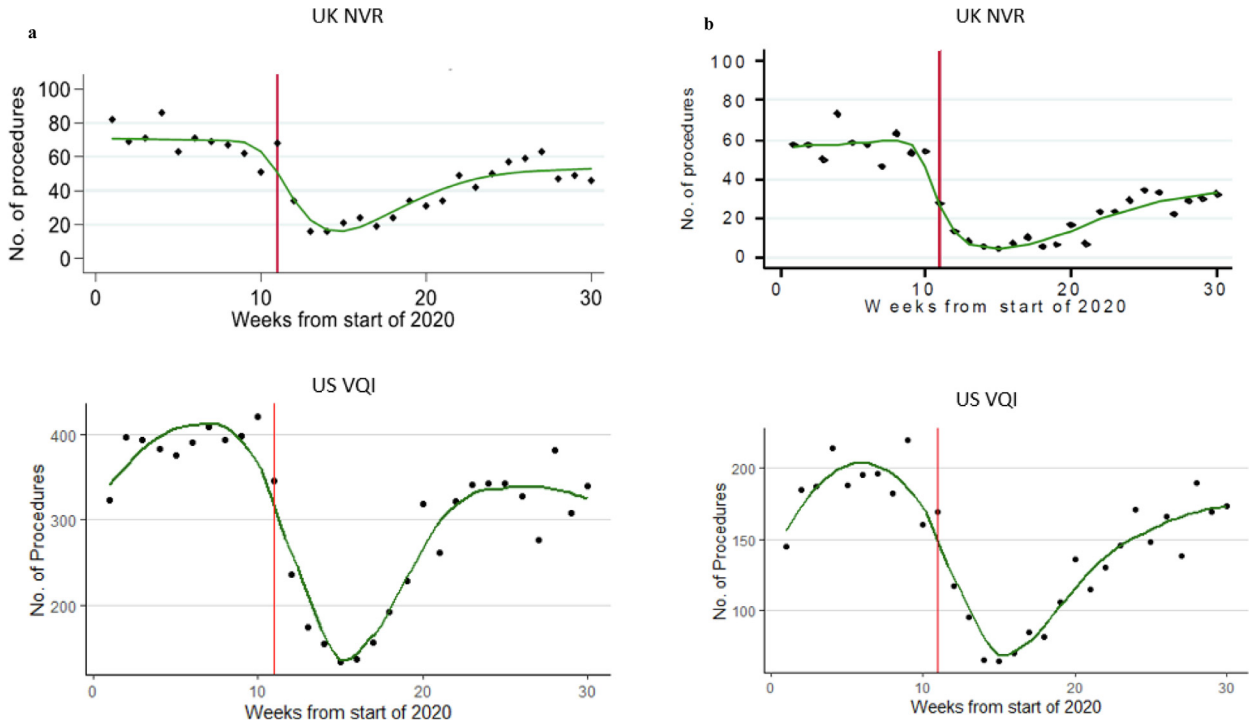

Fig. 1 – (A) UK National Vascular Registry (NVR) and US Vascular Quality Initiative (VQI) comparison: carotid endarterectomy. Weekly number of carotid endarterectomies for first 30 weeks of 2020. Red line denotes week of March 15th. (B) UK NVR and US VQI comparison: infrarenal abdominal aortic aneurysm (AAA) repair. Weekly number of AAA repairs for first 30 weeks of 2020. The red line denotes the week of March 15th. NVR data include elective infrarenal AAA repairs. VQI data include all endovascular aneurysm repair and open procedures.

and 2019 (range, 8% to 53%; median, 14%), as would be expected given the restrictions placed on elective surgery in most countries. This resulted in a higher percentage of nonelective cases (symptomatic) overall in 2020, reflecting fewer elective operations. Elective to nonelective ratios for carotid and venous categories were not included in Table 3, given variable definitions and management within these categories. Differences between registries on asymptomatic carotid interventions performed in the US VQI compared to European registries has been reported previously [28].

Factors likely contributing to this reduction include patient (fear, reluctance to seek care), surgeon (change in AAA size threshold, delay in intervention), resources (bed capacity, staffing), and governance (national/state directives) [26,29]. As local restrictions were lifted by July to August of 2020, procedure volumes gradually approached previous annualized volumes. It remains unclear whether long-term consequences will result in increased adverse patient outcomes. The pandemic provides a unique opportunity to study the natural history of medically managed AAA and symptomatic carotid stenosis. NVR reporting on emergency vascular procedures at the beginning of the pandemic showed declines in ruptured AAA (76%) and major lower limb amputation (83%). This is quite surprising, as these medical catastrophes or urgent operations would not be expected to be significantly impacted. This will require further trend analysis from both registry data and study collaboratives, such as VASCC and COVER.

6. COVID-19 disease-specific collaboratives

In addition to registry data collection, COVID-19 study collaboratives seeking global cooperation and data sharing also emerged in March of 2020. The VASCC is a combined international effort custom-designed for prospective data collection on the impact of vascular surgical care delays and perioperative management of thrombotic complications in patients with COVID-19 infection. VASCC is organized and led by Max Wohlauer, University of Colorado, and Robert Cuff, Michigan State University. De-identified patient information is housed in a REDCap registry at the University of Colorado Anschutz Medical Campus. As of March 2021, 171 centers from 40 countries are involved, including multiple centers from VQI and VASCUNET. VQI and VASCC worked together on harmonization of variables and definitions to optimize future data aggregation and collaboration. VASCC has partnered with CPC Clinical Research in Aurora, CO and Fondazione Policlinico Gemelli Istituto di Ricovero e Cura a Carattere Scientifico in Rome, Italy, to strengthen the international collaboration [30].

VERN also launched the COVER study, sponsored by the Vascular Society of Great Britain and Ireland, a prospective cohort study with data contributed from 251 centers in 53 countries under the direction of Sandip Nandra, Newcastle University and Ruth Benson, University Hospital Coventry [18]. The study was conceived as a three-tier project, focusing on the following different aspects of vascular care:

Table 3 – Registry volumes.

Country	Centers, n[a]	2018 Case volume	2019 Case volume	2020			
				Case volume	Volume change from 2019, %[b]	Elective to nonelective ratio[c]	Mean no. of cases per center
Carotid[d]							
AU	118	1,934	1,793	1,673	93.3		14
NZ	14	303	296	280	94.6		20
SE	20	788	795	778	97.8		39
US	345	21,267	26,435	22,442	84.9		65
Aortic[e]							
AU	114	2,373	2,293	2,034	88.7	2.74	18
NZ	14	459	507	476	93.9	1.93	34
SE	28	1,292	1,339	1,326	99.0	2.75	47
US	235	9,394	9,927	8,363	84.2	4.06	36
Infrainguinal bypass[f]							
AU	111	1,423	1,428	1,278	89.5	1.07	12
NZ	13	293	305	301	98.7	1.12	23
SE	28	1,224	1,134	1,041	91.8	1.21	37
US	182	5,996	6,090	5,758	94.5	3.29	32
Venous[g]							
AU	165	6,235	5,639	3,741	66.3		23
NZ	14	345	365	250	68.5		18
SE	34	10,022	11,317	9,566	84.5		281
US	60	8,395	9,548	7,390	77.4		123

Abbreviations: AU, Australia; NZ, New Zealand; SE, Sweden, US, United States (Vascular Quality Initiative).

[a] No. of centers participating in all 3 years for carotid, aortic, infrainguinal bypass, and venous.

[b] 2020 volumes compared to 2019 (using 2019 as denominator).

[c] Ratio of elective (asymptomatic/routine) procedures divided by nonelective (urgent/emergent) procedures performed in 2020. Symptomatic cases are counted as a nonelective procedure.

[d] Carotid procedures include both carotid endarterectomy/carotid artery stenting.

[e] Aortic includes both endovascular aneurysm repair and open procedures for infrarenal aortic procedures.

[f] Infrainguinal bypass includes lower extremity bypass only.

[g] Venous includes inferior vena cava filter + varicose vein + venous stents.

quantification, analysis, and demonstration of changes to global vascular activity during the course of 2020; in-hospital outcomes following common vascular procedures with subsequent 6- and 12-month follow-up; and changes in the management of consecutive patients presenting with common vascular conditions during the pandemic, including medium- and long-term follow-up. Key COVER findings documented a significant decrease in usual vascular activity, transitioning changes of care to telemedicine, and the avoidance of surgery in presentations other than only the largest aneurysms or most severe arterial occlusive disease. The study has also shown that globally, restricting treatment to more advanced clinical presentations was associated with a marked increase in-hospital overall vascular service mortality at 11%, despite a modest suspected or confirmed COVID-19 infection rate (4%) [18].

As seen in Table 2, study collaboratives can provide a more comprehensive COVID-19 variable data collection than existing registries (which require modification) given the enhanced flexibility of creating de novo data elements specifically targeted at COVID-19. In addition, the study collaboratives focus on the disease rather than the procedure, thereby expanding the inclusion criteria for data collection. In contrast to registries that are procedure-based, study collaboratives are disease-specific and focused. A patient succumbing to an adverse event (ie, disabling stroke or ruptured aneurysm) before receiving an operation will not be included in a procedure-based registry, but would be included into a study collaborative given the inclusion criteria.

However, both VASCC and COVER are limited by voluntary participating centers, in contrast to population-based vascular surgical registries with administrative data infrastructure. Procedure-based registries and study collaboratives can monitor the effects of the pandemic on the overall vascular surgical population from different and broader perspectives. It will be important to cross-link registry data (having established long-term outcomes) with the robust data produced in disease-specific study collaboratives to provide a more comprehensive analysis of the COVID-19 pandemic's effect on vascular disease management and outcomes. The US VQI has 65 centers participating in VASCC, with plans to coordinate data collection and long-term follow-up.

7. Registry outcomes

Most vascular registries collect data on short-term outcomes after procedures, recording lengths of stay, complications, and death within the primary hospitalization or 30 days from operation. Initial data from the COVER study suggest that vascular

surgery in vulnerable patients may have a very high risk for mortality and morbidity [29]. Although the UK NVR COVID-positive rates were only 2.2% on the vascular service (April through July 2020), mortality in patients with AAA and peripheral artery disease and a positive COVID-19 diagnosis was 6.1%, compared to 2.2% in those who were COVID-negative. This was independent of respiratory complications defined as pneumonia, ventilator support > 48 hours, adult respiratory distress syndrome or pulmonary embolism. Mortality of COVID-positive patients experiencing respiratory complications rose to 38.2% compared to those who were COVID-negative at 27.9% [26].

Registries may use cross-matching of data linkage with administrative databases or other health care consortia to determine long-term survival and reintervention. Data accumulation may have a lag time of 1 to 2 years, delaying assessment of procedural outcomes until this process is complete. Use of disease-specific study collaboratives and registry linkage to administrative databases will be required to understand the long-term consequences of COVID-19 infection.

Table 3 indicates a variable effect of the pandemic on overall vascular surgical operation volumes during 2020 ranging from 66% to 99% compared to the previous year. The catch-up effect for vascular surgical interventions after reduced activity during a shutdown or a local viral outbreak of COVID infection will require further analysis. The downstream effect of the pandemic on more selective patient treatment or increased endovascular procedures to reduce length of hospital stay or need for intensive care also requires further detailed assessment.

8. COVID-19 impact on clinical trial research

The importance of scientific research during the COVID-19 pandemic has been highlighted by the dramatic advances made in both the therapeutic management of and the development of vaccines against COVID-19. Vascular surgeons recognized the importance of studying the impact of COVID-19 on vascular patients early in the pandemic and initiatives such as VASCC and COVER are testament to this [31]. However, there is no doubt that COVID-19 has also impacted existing vascular trials. Academicians, research nurses, and other research staff were frequently redeployed to support front-line hospital services at the start of the pandemic, and this resulted in some important trials being halted [32]. The UK-Compass study, a multicenter study on the management of juxtarenal AAAs temporarily paused recruitment in March 2020 and restarted in July 2020 [33]. The reluctance of continuing active trials or initiation of new trials by researchers, manufacturers, and patients must be tempered with concern about undergoing procedures with the confounding impact of COVID-19 on outcomes (eg, stent thrombosis or increased mortality) during the pandemic.

There have been pandemic-influenced positive developments for both registries and research. In the UK, NHS Digital has rapidly developed a Trusted Research Environment that links electronic health records. This initiative led by the Cardiovascular Disease UK Consortium has linked electronic health records from primary care, hospital episodes, death registries and National Clinical Audits with COVID-19 laboratory tests and COVID-19 vaccination data. These linked datasets are already producing important information on the impacts of COVID-19 on cardiovascular disease [34].

9. VASCUNET, VQI, and ICVR

The ICVR was formed as a Medical Device Epidemiology Network (MDEpiNet) coordinated registry network by collaboration of VASCUNET and VQI beginning in 2014, with active participation of representatives from the registries and US Food and Drug Administration. MDEpiNet (www.MDEpiNet.net) is a public–private partnership with international chapters in five countries that brings together health care professionals, industry representatives, patient groups, insurance payers, and governmental agencies to provide a network capable of long-term medical device evaluation and ongoing surveillance. The relationship of MDEpiNet to the ICVR allows for international quality improvement and eventually device evaluation and surveillance. VASCUNET has grown to include 26 regional and national registries in European, South American, and Australasian countries who actively work together to harmonize their registry data collection and pursue collaborative research related to vascular procedures [35].

As has been demonstrated, the impact of the COVID pandemic on each registry within VASCUNET and VQI has been variable, related heavily to the overall prevalence of the virus in each country, the governmental approach to virus containment, the burden on clinical operations, and the impact of personnel who collect data within each registry.

Although ICVR has not yet collected harmonized variables across VASCUNET and VQI, the extensive data collection by both the VQI and numerous registries within VASCUNET will allow for future collaborative projects, similar to what has been reported previously [36,37]. Given the impact of COVID-19 on vascular practice and the high frequency of vascular complications from the virus, the value of worldwide data collection cannot be overstated. The rapid addition and harmonization of variables that has occurred during the pandemic is an exercise that will serve all ICVR-participating registries in the future. Data collection for unexpected and infrequent device failures of this nature in international real-world practice will certainly benefit from the mechanisms that have been established within ICVR related to the pandemic [38].

10. Summary

Registry data has always played an important role in providing real-world data driving clinical practice through quality improvement. It has now become increasingly evident that real-world evidence plays an important role in evaluating real-world problems dynamically. In 2019, the vascular community was disrupted by the Paclitaxel controversy. Registry data helped us better understand the impact of Paclitaxel devices on long-term mortality (Germanvasc, VQI, SwedePAD [Swedish Drug-elution Trial in Peripheral Arterial Disease], Australia/New Zealand, and Spain) [39–42]. In 2020, the vascular community was disrupted by the COVID-19 pandemic.

Again, real-world evidence from registries is helping us better understand the impact and how we should adapt using up-to-date information. Undoubtedly, there will be future events or pandemics where registry data and real-world evidence will help us to better respond in a timely manner. We must prepare our clinical and administrative registries to be adaptable, responsive, and use active surveillance monitoring to identify signal detection or address future unknown events. As a first important step, the responsible consortia implemented corresponding codes to identify patients with positive SARS-CoV-2 infection in registry and administrative data. This emphasizes that events with enough impact can lead to changes in an often-rigid environment. The vascular community would be well advised to use the momentum noted and discuss the implementation of unique device identifiers into administrative data to be prepared for future tasks and challenges.

REFERENCES

[1] Natarajan JP, Mahenthiran AK, Bertges DJ, et al. Impact of COVID-19 on the Society for Vascular Surgery Vascular Quality Initiative Arterial Procedure Registry. J Vasc Surg 2021 Feb 3 [Epub ahead of print]. doi:10.1016/j.jvs.2020.12.087.

[2] Mahenthiran AK, Natarajan JP, Bertges DJ, et al. Impact of COVID-19 on the Society for Vascular Surgery Vascular Quality Initiative Venous Procedure Registries (varicose vein and inferior vena cava filter). J Vasc Surg Venous Lymphat Disord 2021 Jan 19 [Epub ahead of print]. doi:10.1016/j.jvsv.2021.01.002.

[3] Seiffert M, Brunner FJ, Remmel M, et al. Temporal trends in the presentation of cardiovascular and cerebrovascular emergencies during the COVID-19 pandemic in Germany—an analysis of health insurance claims. Clin Res Cardiol 2020;109:1540–8.

[4] Davis S, Pai S. Challenges and opportunities for sponsors in conducting clinical trials during a pandemic. Perspect Clin Res 2020;11:115–20.

[5] Upadhaya S, Yu JX, Oliva C, et al. Impact of COVID-19 on oncology clinical trials. Nat Rev Drug Discov 2020;19:376–7.

[6] Tagliafico AS, Albano D, Torri L, et al. Impact of coronavirus disease 2019 (COVID-19) outbreak on radiology research: an Italian survey. Clin Imaging 2021;76:144–8.

[7] Pritchard A. Reducing burden and releasing capacity at NHS providers and commissioners to manage the COVID-19 pandemic. Available at: https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/03/C0113-reducing-burden-and-releasing-capacity-at-nhs-providers-and-commissioners.pdf. Accessed Jan 10, 2021.

[8] Gabutti G, d'Anchera E, Sandri F, et al. Coronavirus: update related to the current outbreak of COVID-19. Infect Dis Ther 2020;9(2):1–13.

[9] Libby P, Luscher T. COVID-19 is, in the end, an endothelial disease. Eur Heart J 2020;41:3038–44.

[10] Putko RM, Bedrin MD, Clark DM, et al. SARS-CoV-2 and limb ischemia: a systematic review. J Clin Orthop Trauma 2021;12:194–9.

[11] Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol 2020;77:683–90.

[12] Li YC, Bai WZ, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. J Med Virol 2020;92:552–5.

[13] American College of Surgeons. COVID-19 guidelines for triage of vascular surgery patients. Available at: www.facs.org/covid-19/clinical-guidance/elective-case/vascular-surgery. Accessed Jan 10, 2021.

[14] Forbes TL. Vascular surgery activity condition is a common language for uncommon times. J Vasc Surg 2020;72:391–2.

[15] Mouawad N, Woo K, Malgor R, et al. The impact of the COVID-19 pandemic on vascular surgery practice in the United States. J Vasc Surg 2021;73:772–9.

[16] Shalhub S, Mouawad NJ, Malgor RD, et al. Global vascular surgeons' experience, stressors, and coping during the coronavirus disease 2019 pandemic. J Vasc Surg 2021;73:762–71 .e4.

[17] Aziz F, Bath J, Smeds M. Implications of the severe acute respiratory syndrome associated with the novel coronavirus-2 on vascular surgery practices. J Vasc Surg 2021;73:4–11 .e2.

[18] Vascular and Endovascular Research Network (VERN) COVER study collaborativeGlobal impact of the first coronavirus disease 2019 (COVID-19) pandemic wave on vascular services. Br J Surg 2020;107:1396–400. https://vascular-research.net/projects/cover-study-COVID-19-vascular-service-study Accessed Feb 18, 2021.

[19] Kolata G. Amid the coronavirus crisis, heart and stroke patients go missing. New York Times April 25, 2020. Available at: https://www.nytimes.com/2020/04/25/health/coronavirus-heart-stroke.html PublishedUpdated November 2, 2020. Accessed May 13, 2021.

[20] Siu M, Lin A, Narvaez V, et al. Analysis of outcomes in acute limb ischemia patients during COVID-19 State of Emergency in Western Massachusetts. J Vasc Surg 2021;73:38–9.

[21] Nypaver T, Miller D, Weaver M, et al. Symptomatic extracranial carotid disease in COVID-19 patients is related to thrombus formation. J Vasc Surg 2021;73:44–5.

[22] Ilonzo N, Rao A, Safir S, et al. Acute thrombotic manifestations of coronavirus disease 2019 infection: experience at a large New York City health care system. J Vasc Surg 2021;73:789–96.

[23] Demelo-Rodriguez P, Ordieres-Ortega L, Zichen J, et al. Long-term follow up of patients with venous thromboembolism and COVID-19: analysis of risk factors for death and major bleeding. Eur J Haematol 2021;105:716–23.

[24] COVID-19 virus and vascular surgery. Vascular Society Great Britain and Ireland 27th March 2020. Available at: https://www.vascularsociety.org.uk/_userfiles/pages/files/Newsletters/2020/Presidents%20update%2027_03_20.pdf Accessed Jan 10,2021.

[25] World Health OrganizationConsiderations for implementing and adjusting public health and social measures in the context of COVID-19. Interim Guidance- 4 November 2020. WHO reference number: WHO/2019-nCoV/Adjusting_PH_measures/2020.2. Available at: https://www.who.int/publications/i/item/considerations-in-adjusting-public-health-and-social-measures-in-the-context-of-covid-19-interim-guidance Accessed May 13, 2021.

[26] Impact of the Covid-19 pandemic on the provision of vascular surgery in the UK National Health Service. National Vascular Registry Short Report. November 2020. Available at: https://www.vsqip.org.uk/content/uploads/2020/11/NVR-Short-Report-Covid-19.pdf. Accessed Jan 10, 2021.

[27] Ball S, Banerjee A, Berry CCVD-COVID-UK Consortium. Monitoring indirect impact of COVID-19 pandemic on services for cardiovascular diseases in the UK. Heart 2020;106:1890–7.

[28] Venermo M, Wang G, Sedrakyan A, et al. Carotid stenosis treatment: variation in international practice patterns. Eur J Vasc Endovasc Surg 2017;53:511–19.

[29] Benson RA, Nandhra S. Outcomes of vascular and endovascular interventions performed during the coronavirus disease 2019 (COVID-19) pandemic. Ann Surg 2021;273:630–5.

[30] Mouawad NJ, Cuff RF, Hultgren R, et al. The Vascular Surgery COVID-19 Collaborative (VASCC). J Vasc Surg 2020;72:379–80. Available at: https://medschool.cuanschutz.edu/surgery/specialties/vascular/research/vascular-surgery-covid-19-collaborative/vascc Accessed Feb 18, 2021.

[31] Björck M, Boyle JR, Dick F. The need of research initiatives amidst and after the Covid-19 Pandemic: a message from the editors of the EJVES. Eur J Vasc Endovasc Surg 2020;59:695–6.
[32] Le Breton S, Lamberti MJ, Dion A, et al. COVID-19 and its impact on the future of clinical trial execution. Appl ClinTrials October 22, 2020. Available at: https://www.appliedclinicaltrialsonline.com/view/covid-19-and-its-impact-on-the-future-of-clinical-trial-execution Published Accessed May 13, 2021.
[33] A comparison of open surgery, minimal invasive surgery and medical management for complex aortic aneurysms. ISRCTN85731188. Available at: 10.1186/ISRCTN85731188. Accessed Feb 18, 2021.
[34] Wood A, Denholm R, Hollings S, et al. Linked electronic health records for research on a nationwide cohort including over 54 million people in England. From CVD-COVID-UK Consortium. BMJ 2021;373:n826.
[35] Beck AW, Sedrakyan A, Mao J, et al. International Consortium of Vascular Registries. Variations in abdominal aortic aneurysm care: a report from the International Consortium of Vascular Registries. Circulation 2016;134:1948–58.
[36] Behrendt CA, Sigvant B, Kuchenbecker J, et al. Editor's choice—international variations and gender disparities in the treatment of peripheral arterial occlusive disease—a report from VASCUNET and the International Consortium of Vascular Registries. Eur J Vasc Endovasc Surg 2020;60:873–80.
[37] Scali ST, Beck AW, Sedrakyan A, et al. Hospital volume association with abdominal aortic aneurysm repair mortality—-analysis of the International Consortium of Vascular Registries. Circulation 2019;140:1285–7.
[38] Sutzko D.C., Mani K., Behrendt C.A., et al. Big data in vascular surgery: registries, international collaboration and future directions. J Intern Med 288:51–61.
[39] Behrendt CA, Bertges D, Eldrup N, et al. International Consortium of Vascular Registries consensus recommendations for peripheral revascularization registry data collection. Eur J Vasc Endovasc Surg 2018;56:217–37.
[40] Heidemann F, Peters F, Kuchenbecker J, et al. Long-term outcomes after revascularizations below the knee with paclitaxel-coated devices—a propensity score matched cohort analysis. Eur J Vasc Endovasc Surg 2020;60:549–58.
[41] Behrendt CA, Sedrakyan A, Peters F, et al. Editor's choice—long term survival after femoropopliteal artery revascularizations with paclitaxel-coated devices—a propensity score matched cohort analysis. Eur J Vasc Endovasc Surg 2020;59:587–96.
[42] Bertges DJ, Sedrakyan A, Sun T, et al. mortality after paclitaxel coated balloon angioplasty and stenting of superficial femoral and popliteal artery in the Vascular Quality Initiative. Circ Cardiovasc Interv 2020;13(2):e008528.