Arterial blood gas analysis: as safe as we think? A multicentre historical cohort study

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Shareable abstract (@ERSpublications)
Arterial punctures for arterial blood gas analysis are safe procedures with a major complication rate within 7 days of 0.14% (95% CI 0.13–0.15%). Patients on antithrombotic medication have an increased risk of developing major complications. https://bit.ly/3FaPOwk

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Abstract
Purpose Arterial punctures (APs) for arterial blood gas (ABG) analyses are much-used medical procedures. To date, no large studies have been conducted on the major complication rate of APs. We aimed to describe the risk of major complications within 7 days after puncture and investigate whether using antithrombotic medication affected this.

Methods We included all APs performed for ABG analysis at three Danish hospitals from January 1, 1993 to February 25, 2013. We excluded APs ordered by the anaesthesiology department, intensive care unit (ICU) or in patients <18 years old. Data on the patient level were extracted from the Danish National Patient Registry, Danish Civil Registration System and Odense Pharmaco-Epidemiologic Database (OPED), the latter providing us with information on antithrombotic medication. Initially, two clinicians compiled a list with all procedures and diagnoses that could possibly be a consequence of APs. The selected procedures and diagnoses were further categorised independently by three surgeons and used to indicate the complication rate.

Results We analysed 473,327 APs and found 669 (0.14%, 95% CI 0.13–0.15) APs led to major complications: embolisms or thrombosis (49.0%), aneurysms (15.4%), nerve damage (1.5%), arteriovenous fistulas (0.6%) or of another kind (33.5%). The identified major complication rates in patients on antithrombotic medication were increased (OR 1.31, 95% CI 1.07–1.61).

Conclusion APs for ABG analyses are safe procedures. The major complication rate within 7 days was 0.14% (95% CI 0.13–0.15). Patients on antithrombotic medication carry an increased risk of developing major complications.

Introduction
Sampling for arterial blood gas (ABG) analysis is a well-known and much-used invasive procedure applied within hospital departments on a daily basis. It is of importance in diagnosing and assessing acutely ill patients, easy to perform and can be executed by doctors, nurses and laboratory technicians [1, 2]. In addition, sampling is possibly painful and distressing because of the highly innervated sampling locations and occasional multiple attempts [3–5]. Contraindications are relative and strict and a standard protocol should be followed, all with the aim of reducing technical difficulties and possible harm done to the patient [6, 7].

The assumption that arterial punctures (APs) are safe is generally based on small, fairly out-dated studies that mainly focus on minor complications. For example, 4342 APs obtained in a military setting from 1969...
to 1970 resulted in 25 haematomas (0.58%), none of which were defined as a major complication [8]. A study using computed tomography scans revealed haematoma formation in 128 out of 270 patients (47.4%), none of which progressed to a severe condition [9]. Another study of 6185 brachial artery punctures found an overall incidence of complications of 2.0%, varying from immediate limb pain or paresthesia to haematoma formation. Again, none of the complications were considered to be major [10]. All of the previously found minor complications resolved spontaneously [8–10]. Major complications have generally been defined as leading to prolonged hospitalisation time or a need for surgical treatment or another intervention due to ischaemia or other objective abnormalities [8–12]. Described major complications include thrombosis with distal ischaemia, major haemorrhages and haematomas, (pseudo) aneurysms, nerve damage and arteriovenous fistulas. The largest published study, reporting numbers on these major complications, included 266 punctures: the previously mentioned major complications occurred in 3.6% to 10.3% of the APs [11]. A study from 1967 found that 19 out of 1466 (1.3%) percutaneous needle punctures led to major complications, thrombosis at the entry site with distal ischaemia being the most common [12]. Similar and other unique complications such as an arteriovenous fistula leading to pulmonary oedema and a small bowel perforation due to femoral herniation have been reported in a number of case reports [13–20].

Overall, major complications can occur, but studies show variety in the incidence of complications, and sample sizes are too small to make inferences about the occurrence of the different types of major complications. Although complications may be limited, a serious complication such as thrombosis may have dire consequences for the patient. This particular topic needs to be studied in further detail. An AP is a routinely performed procedure and complications are not taken into consideration, since it is unclear what the consequences are and at what rates they occur. In addition, little is known about the risk of major complications in patients on antithrombotic medication [12, 19, 21, 22].

The primary aim of this paper is to assess the incidence of major complications, 7 days after APs for ABG analyses. Our secondary aim is to analyse whether patients on antithrombotic medication prior to hospitalisation have a higher complication rate. Our hypothesis is that there is a very low major complication rate within 7 days after arterial blood sampling for an ABG. We expect the major complication rate to be comparable in patients on and off antithrombotic medication.

Methods
This paper is reported in conjunction with the RECORD Guidelines [23]. This study was approved by the Danish Data Protection Agency (approval number 2008-50-0035) and the Danish National Board of Health (approval number 3-3013-122/1). The regional Ethics Committee on science confirmed that the project did not require approval according to Danish law.

Study design
We performed a multicentre historical cohort study with prospectively collected data that were analysed retrospectively.

Setting
Data were collected from three hospitals in the region of Southern Denmark (Hospital of South West Jutland; Hospital Lillebaelt; Odense University Hospital) on all ABGs between January 1, 1993 and February 25, 2013.

Participants
All adult patients (>18 years) with a Danish unique identifying “Central Persons Register” (CPR) number with a registered ABG within the study period were included. APs were excluded if the ABG was ordered by the intensive care unit (ICU) or the anaesthesiology department, because these samples were possibly drawn from indwelling arterial catheters. Since this study had a short follow-up time, we assumed no patients emigrated within 7 days after the AP and therefore did not exclude patients based on this element.

Variables
The variables used in this study on patient level were age, sex and Charlson Comorbidity Index (CCI), the latter categorised as CCI score of 0, 1, 2 or ≥3. The CCI was used to describe the degree of comorbidity in patients [24, 25]. This study analysed every puncture separately because we wanted to know how many APs led to a major complication. The primary outcome was the occurrence of major complications within 7 days after the AP, which were defined as a procedure or diagnosis registered in the national registries with respectively Sundheds-væsenets Klassifikations System (SKS) or International Classification of
Diseases (ICD) codes that could have been the result (i.e. a proxy) of the complication. The secondary outcome was the major complication rate in patients on antithrombotic medication.

Data sources/measurement
Data on patient level were extracted from the Danish National Patient Registry, the Danish Civil Registration System and the Odense Pharmaco-Epidemiologic Database (OPED). Information on prior, current and later hospitalisations was requested from the Danish National Patient Registry and follow-up information on vital status from the Danish Civil Registration System [26, 27]. All the registered procedures and diagnoses in the patients who had an ABG ordered were listed. This list included both SKS codes (NOMESCO codes – Scandinavian standard procedure codes) and ICD-8 and ICD-10 codes (codes for diagnoses) [27]. SKS codes are registered at the time of the procedure; ICD codes are registered at the time of transfer between wards or at hospital discharge. Information about prescribed antithrombotic medication (anticoagulant and antiplatelet medication) prior to hospitalisation was received from the OPED, which was used to register patients who had reimbursed a prescription within 90 days before the AP [28, 29].

Bias
A description of the efforts made to address potential sources of bias is described under the heading Quantitative variables.

Study size
The study size was arrived at by including all available data on our topic of interest within the study period.

Quantitative variables
Two of the authors – a cardiologist and a clinical pharmacologist (M.B. and D.P.H.) – independently went through the list of SKS, ICD-8 and ICD-10 codes and excluded all procedures and diagnoses that were clearly irrelevant to our study (e.g. caesarean section or hip replacement), resolving disagreement by oral consensus. To create the most accurate description of possible complications, three independently blinded surgeons – one orthopaedic surgeon (B.V.) and two vascular surgeons (C.H. and J.S.L.) – assessed the selected procedures and diagnoses and classified them as “Very likely”, “Possible but unlikely” and “Not possible” to be the result of an AP (see table 1 for a list of all the SKS, ICD-8 and ICD-10 codes that were included by the two authors, and how they were categorised by the surgeons). In the analyses, all the procedures or diagnoses that were marked by at least one of the surgeons as “Very likely” were included as being a major complication, thus giving the realistic complication rate. All procedures and diagnoses marked as “Very likely” or “Possible but unlikely” were included to indicate the maximum complication rate. Because both SKS and ICD codes were used, codes registering the same (type of) complication were clustered through assessment by the two authors: five major complication categories were identified, as shown in table 2.

Statistical methods
Statistical analysis was performed using Stata/IC 15.0 (Stata Corp, College Station, TX, USA). Data are presented as medians (range) or proportions (95% confidence interval), since the data were not with a normal distribution. The effect of sex, age, use of antithrombotic medication, CCI and number of prior APs was examined in an unmatched logistic regression and shown with adjusted and unadjusted odds ratios. If information on the CCI was missing, we assumed that the patient did not have any relevant comorbidity. We counted the number of APs in the 7 days prior to the AP that we assumed led to a complication. We only used the last AP on that day. To describe the effect of usage of antithrombotic medication prior to receiving an AP, a chi-square test was used.

Data access and clearing methods
All authors had full access to the database population which was used to create the study population. As data were extracted from national databases, no additional cleaning was required.

Linkage
Denmark has unique identifying numbers – Central Persons Register (CPR) numbers – making complete follow-up and true population-based studies possible [26, 27]. The Danish unique identifying CPR numbers were used to link the available data from the multiple databases used within this study.

Results
Demographics
From January 1, 1993 to February 25, 2013, 975 360 ABGs were ordered in the three participating hospitals. We included a total of 473 327 APs (figure 1), which were performed in 109 696 patients. Some
| Code          | Very likely | Possible but unlikely | Not possible |
|--------------|-------------|-----------------------|--------------|
| 44299 – Aneurysm arteria aliud | X           |                        | XX           |
| 44441 – Embolism, thrombosis arteria femoralis | X           |                        | XX           |
| 44442 – Embolism, thrombosis arteria popliteae | X           |                        | XX           |
| 44444 – Embolism, thrombosis arteria peripheriae extremitatis | X           |                        | XX           |
| 68220 – Inflammation, abscess and acute lymphangioma. brachii and antebrachii | X           |                        | XX           |
| 95209 – Traumatic lesion plexus brachialis and nervi brachii, uncomplicated | X           |                        | XX           |
| DG560 – Carpal tunnel syndrome | X           | X                      | XX           |
| DG562 – Neuropathy in nervus ulnaris | XXX         |                        |              |
| DT721 – Aneurysm upper extremity | X X         |                        | X            |
| DT721 – Aneurysm in artery in upper extremity | X X         |                        | X X          |
| DT724 – Aneurysm in artery in lower extremity | X X         |                        | X            |
| DT729 – Aneurysm unspecified | X X         |                        | X            |
| DT742 – Embolism or thrombosis in artery in upper extremity | X X         |                        | X            |
| DT742A – Embolism or thrombosis in upper extremity | X X         |                        | X X          |
| DT742A – Emboli arteria brachialis | X           |                        | XX           |
| DT742B – Thrombosis in artery in upper extremity | X X         |                        | X            |
| DT742B – Thrombosis arteria brachialis | X X         |                        | X            |
| DT743 – Embolism or thrombosis in artery in lower extremity | X X         |                        | X            |
| DT743A – Embolism in artery in lower extremity | X X         |                        | X X          |
| DT743B – Thrombosis in artery in lower extremity | X X         |                        | X X          |
| DT744 – Embolism or thrombosis in artery unspecified extremity | X           |                        | X X          |
| DT748 – Embolism or thrombosis in other artery | X           |                        | XX           |
| DT749 – Embolism or thrombosis in artery unspecified | X           |                        | XX           |
| DT770 – Acquired A-V fistula | X X         |                        | X            |
| DT771 – Artery stricture | X           |                        | X            |
| DT771 – Stricture of artery | XX          |                        |              |
| DT772 – Artery rupture | XXX         |                        |              |
| DT775 – Artery necrosis | X           |                        | XX           |
| DI803A – Embolism in lower extremity unspecified | X           |                        | XX           |
| DM622A – Non-traumatic compartment syndrome | XXX         |                        |              |
| DS451 – Lesion of arteria brachialis | X X         |                        | X            |
| DS540 – Lesion of nervus ulnaris in elbow region or lower arm | X X         |                        | XX           |
| DS541 – Lesion of nervus medianus in elbow region or lower arm | X           |                        | X            |
| DS542 – Lesion of nervus radialis in elbow region or lower arm | X           |                        | XX           |
| DS550 – Lesion of nervus ulnaris in elbow region or lower arm | X X         |                        | X            |
| DS551 – Lesion of arteria radialis in elbow region or lower arm | X X X       |                        |              |
| DS561 – Lesion of muscle/tendon of long flexor to a finger on lower arm | X           |                        | XX           |
| DS562 – Lesion of muscle or tendon of other flexor on lower arm | X           |                        | XX           |
| DS568 – Lesion of an unspecified muscle or tendon in elbow/lower arm | X           |                        | XX           |
| DS641 – Lesion of nervus medianus in wrist or hand | X X         |                        | X            |
| DS659 – Lesion of blood vessel in wrist or hand unspecified | X X         |                        | X            |
| DS660 – Lesion of long flexors to thumb in wrist/hand | X X         |                        | XX           |
| DS661 – Lesion of flexors to unspecified finger in wrist or hand | X           |                        | XX           |
| DS750 – Lesion in arteria femoralis | X           |                        | XX           |
| DT145 – Lesion in blood vessel without indication of body region | X           |                        | X X          |
| DT801 – Complication in vessel after infusion, transfusion on injection | X X         |                        | X            |
| DT802 – Infection after infusion, transfusion or injection | X X         |                        | X            |
| DT808 – Other complication after infusion, transfusion or injection | X X         |                        | X X          |
| DT809 – Complication after infusion, transfusion or injection unspecified | X X         |                        | X            |
| DT812K – Inadvertent preoperative puncture/lesion of vein or lymph system | X X         |                        | X            |
| DT814 – Infection after intervention unspecified | X X         |                        | X            |
| DT817 – Complication in vessel after intervention unspecified | X X         |                        | X            |
| DT817B – Thromboembolic complication unspecified | X X         |                        | X            |
| DT817K – Thrombosis, embolism or necrosis after vessel operation | X X         |                        |              |
| DT819 – Complication of procedure unspecified | X           |                        | XX           |
| DT88 – Complications from surgery | X           |                        | X            |
| DT888 – Complication with surgery or with unspecified treatment, other specified | X X         |                        | XX           |
| KACA11 – Exploration, n. medianus | X           |                        | XX           |

Continued
### Table 1 Continued

| Code     | Very likely | Possible but unlikely | Not possible |
|----------|-------------|-----------------------|--------------|
| KACA13   |             |                       | X            |
| KACC51   | X           | X                     | X            |
| KACC53   | X           | X                     | X            |
| KNCM99   |             |                       | XXX          |
| KNDA02   |             |                       | X            |
| KNDA05   |             |                       | X            |
| KNDA10   |             |                       | X            |
| KQCA00   | X           | X                     | X            |
| KQCA05   |             |                       | X            |
| KQCA10   |             |                       | X            |
| KQCB00   | X           | X                     | X            |
| KQCB05   |             |                       | X            |
| KQCB10   |             |                       | X            |
| KQCB99   |             |                       | X            |
| KTNC00   |             |                       | X            |
| KTNC05   |             |                       | X            |
| KTND00   |             |                       | X            |
| KTND05   |             |                       | X            |

### Table 2

| Code     | Category                                      |
|----------|-----------------------------------------------|
| DI742    | Embolism or thrombosis in artery in upper extremity |
| DI743    | Embolism or thrombosis in artery in lower extremity |
| DI743A   | Embolism in artery in lower extremity         |
| DI743B   | Thrombosis in artery in lower extremity       |
| DI744    | Embolism or thrombosis in artery in unspecified extremity |
| DI749    | Embolism or thrombosis in artery unspecified |
| 44441    | Embolism, thrombosis arteria femoralis        |
| 44442    | Embolism, thrombosis arteria popliteae        |
| 44444    | Embolism, thrombosis arteria periphericae extremitatis |
| DT721    | Aneurysm upper extremity                      |
| DT721    | Aneurysm in artery in upper extremity         |
| DT724    | Aneurysm in artery in lower extremity         |
| DT729    | Aneurysm unspecified                          |
| 44299    | Aneurysm arteria aliud                        |
| DS541    | Lesion of nervus medianus in elbow region or lower arm |
| DS5641   | Lesion of nervus medianus in wrist or hand    |
| DI770    | Acquired A-V fistula                          |
| DI550    | Lesion of nervus ulnaris in elbow region or lower arm |
| DI5750   | Lesion in arteria femoralis                   |
| DT145    | Lesion in blood vessel without indication of body region |
| DT801    | Complication in vessel after infusion, transfusion or injection |
| DT808    | Other complication after infusion, transfusion or injection |
| DT809    | Complication after infusion, transfusion or injection unspecified |
| DT812K   | Inadvertent preoperative puncture/lesion of vein or lymph system |
| DT817    | Complication in vessel after intervention unspecified |
| DT88     | Complications with or with surgery            |
| DT888    | Complication with surgery with unspecified treatment, other specified |
| 68229    | Inflammation, abscess and acute lymphangioma. brachii and antebrachii |

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51.3% of the APs were performed in males (n=242,867). The median age at the time of the AP was 69 years (IQR 58–77 years). 28.4% of the APs were performed in patients with a CCI score of 0, 45.1% in patients with a CCI score of 1–2 and 26.5% at a CCI score of ≥3 (table 3).

Complications

Major complications occurred after 669 out of 473,327 APs (0.14%, 95% CI 0.13–0.15). The complications occurred in 303 patients (0.28%, 95% CI 0.25–0.31). The majority of complications occurred in males (59.8%, n=400). The median age at the time of the AP leading to a major complication was 69 years (IQR 61–76). A total of 28.7% of the APs with a major complication were performed in patients with a CCI score of 0, 44.8% in patients with a CCI score of 1–2 and 26.5% at a CCI score of ≥3 (table 4).

Figure 2 shows the percentage of APs per year from 1993 to 2013 leading to a major complication, as a total and by sex. The major complication rate tends to show a slight decrease over the years, with the highest rate in 1993.

| TABLE 3 | Baseline characteristics of patients having an arterial blood gas drawn in the period from January 1, 1993 to February 25, 2013 |

|                | Total punctures | Age 18–64 years | Age 65–79 years | Age ≥80 years |
|----------------|-----------------|-----------------|-----------------|---------------|
| Total n        | 473,327         | 177,978         | 205,228         | 90,121        |
| Age years      |                 |                 |                 |               |
| Male           | 424,867 (51.3)  | 95,811 (53.8)   | 104,995 (51.2)  | 42,061 (46.7) |
| Female         | 230,460 (48.7)  | 82,167 (46.2)   | 100,228 (48.8)  | 48,060 (53.3) |
| Charlson Comorbidity Index |                     |                 |                 |               |
| 0              | 134,514 (28.4)  | 74,310 (41.8)   | 40,733 (19.8)   | 19,471 (21.6) |
| 1              | 126,142 (26.7)  | 45,325 (25.5)   | 58,337 (28.4)   | 22,480 (24.9) |
| 2              | 87,244 (18.4)   | 24,101 (13.5)   | 43,246 (21.1)   | 19,897 (22.1) |
| ≥3             | 125,427 (26.5)  | 50,449 (17.3)   | 83,863 (26.4)   | 30,586 (30.5) |
| Data presented as n (%) and median (IQR) unless otherwise stated. |       |                 |                 |               |
The categories of major complications were embolisms or thrombosis (49.0%), aneurysms (15.4%), nerve damage (1.5%), arteriovenous fistulas (0.6%) or of another kind (33.5%), such as lesion of an artery (table 5).

**Antithrombotic medication**

A total of 70,422 APs (14.9%) were performed in patients who fulfilled a prescription of at least one type of antithrombotic medication (respectively anticoagulant or antiplatelet treatment), within 90 days prior to the AP. As shown in figure 1 and table 6, the complication rates per AP were comparable; respectively 0.14% (95% CI 0.12–0.15) in APs in patients without antithrombotic use and 0.17% (95% CI 0.14–0.21) in APs in patients with antithrombotic use. We found a statistically significant difference in complication rates in APs in patients on and off antithrombotics (p=0.02). We did not find a statistically significant difference in complication rates when comparing APs in patients using three different medication subgroups: use of one anticoagulant, use of one antithrombotic and use of ≥2 types of antithrombotic medication (p=0.11) (table 6).

**Risk factors**

We found, when adjusted for age, sex, CCI and use of antithrombotic medication, the only variables associated with an increased risk of developing a major complication are male sex (OR 1.41, 95% CI 1.20–1.64) and using antithrombotic medication (OR 1.31, 95% CI 1.07–1.61) (table 7). All other analysed risk factors were not significant. All the possible confounders were predefined as potentially clinically relevant.

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**TABLE 4** Baseline characteristics of patients with a major complication after a puncture for an arterial blood gas was performed in the period from January 1, 1993 to February 25, 2013

| Total punctures | Age 18–64 years | Age 65–79 years | Age ≥80 years |
|-----------------|-----------------|----------------|---------------|
| Total n         | 669             | 255            | 300           | 114           |
| Age years       | 69 (61–76)      | 55 (48–63)     | 74 (68–76)    | 83 (82–87)    |
| Sex             |                 |                |               |               |
| Male            | 400 (59.8)      | 155 (60.8)     | 192 (64.0)    | 53 (46.5)     |
| Female          | 269 (40.2)      | 100 (39.2)     | 108 (36.0)    | 61 (53.5)     |
| Charlson Comorbidity Index |           |                |               |               |
| 0               | 192 (28.7)      | 71 (27.8)      | 92 (30.7)     | 29 (25.4)     |
| 1               | 201 (30.0)      | 95 (37.3)      | 91 (30.3)     | 15 (13.2)     |
| 2               | 99 (14.8)       | 40 (15.7)      | 34 (11.3)     | 25 (21.9)     |
| ≥3              | 177 (26.5)      | 49 (19.2)      | 83 (27.7)     | 45 (39.5)     |

Data presented as n (%) and median (IQR) unless otherwise stated.

The categories of major complications were embolisms or thrombosis (49.0%), aneurysms (15.4%), nerve damage (1.5%), arteriovenous fistulas (0.6%) or of another kind (33.5%), such as lesion of an artery (table 5).

**FIGURE 2** Percentage of arterial punctures leading to a major complication, stratified by sex and year in three hospitals in Denmark from 1993 to 2013.
Maximum complication rate

From the 473,327 analysed, 1,762 APs (0.37%, 95% CI 0.36–0.39) led to a major complication when calculating the maximum complication rate, an overestimation of the actual major complication rate. In this consideration the complications occurred in 633 patients (0.58%, 95% CI 0.53–0.62).

Discussion

In this multicentre historical cohort study, we analysed 473,327 APs and found them to be safe: they have a low major complication rate, with 0.14% (95% CI 0.13–0.15) of the APs leading to major complications (i.e. embolisms or thrombosis, aneurysms, nerve damage, arteriovenous fistulas or of another kind). Patients on antithrombotics are associated with an increased risk of developing major complications (0.17%, 95% CI 0.14–0.21). The only variables associated with an increased risk of developing a major complication after an AP are male sex and using antithrombotic medication.

This is the first large study on this topic: comparisons with existing studies are restricted since they are relatively small. Previously reported major complication rates were low, although the occasional registered major complications and single case reports show that major complications can occur, which is in accordance with our findings [9, 10, 12]. Research with a database as large as ours allows insight into the actual incidence of these major complications. Women seemed to have a higher complication rate in 1993, but we cannot clarify why. This study additionally provides evidence that patients on antithrombotics have an increased complication rate (p=0.02). When further stratified by type and number of antithrombotic medication and comparing four groups, no significant difference (p=0.11) was found. Our findings disagree with the only study we found on this topic which reported that patients on anticoagulants had over four times more complications (both minor and major). That study included punctures for arterial entry, catheterisation and arteriotomy [12]. Concerning the difference in risk related to sex, no similar bibliographic records have been found. ISSII et al. (2012) [9] found no significant difference between complications in males and females; no other studies reported on this outcome variable. This study does not provide an answer to the question why male sex is associated with an increased complication rate. Moreover, the finding that in the period 1993–1994 more complications were recorded in women was probably due to statistical variation. Our study provides evidence that the number of APs performed in the prior 7 days does not increase the adjusted odds ratio on developing a major complication (OR 0.89, 95% CI 0.76–1.04). This is in agreement with the only other study on APs reporting on this variable [30].

To establish a causal relationship with major complications as defined here, a different kind of study set-up has to be used. Access to individual medical records would be required to investigate every patient with an AP that presumably led to a complication. This would however not increase the risk estimate. It would only lead to exclusion of events that are, at present, labelled as complications. Moreover, as we did not

| TABLE 6 | Arterial punctures leading to a major complication in patients on and off antithrombotic medication, further stratified by type and number of antithrombotic medications |
| --- | --- |
| | No complications n (%), 95% CI | Complications n (%), 95% CI | p-value |
| Total n | 472,658 (100) | 669 (100) |
| Antithrombotic medication – | 402,357 (85.1, 85.0–85.2) | 548 (81.9, 78.8–84.8) |
| Antithrombotic medication + | 70,301 (14.9, 14.8–15.0) | 121 (18.1, 15.2–21.2) | 0.02 |
| 1 anticoagulant | 9776 (2.1, 2.0–2.1) | 19 (2.8, 1.7–4.4) |
| 1 antiplatelet | 33,501 (7.1, 7.0–7.2) | 58 (8.7, 6.6–11.1) |
| 2 antithrombotics | 27,035 (5.7, 5.7–5.8) | 44 (6.6, 4.8–8.7) | 0.11 |

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have access to the medical records, it was impossible to assess that the procedure did not endanger the lives of the patients to whom it was applied. As far as we can see, there were no life-threatening complications reported. Unfortunately, it is not possible to distinguish between two APs performed within a very short period of time: we simply do not know which one led to the assumed complication. Another challenging task for further research is analysing utilisation patterns of ABGs. A study attempting this topic found 27.6% of ABGs were ordered as routine, with 79% of the results being as expected \[1\]. However, these results led to a change in patient management in only 42% of the cases. This shows that fewer ABGs can be performed. Providing more insight into these patterns creates clinical awareness of the utilisation of ABGs and could influence clinical decision-making: potentially fewer ABGs could be performed, decreasing risk exposure and costs. Finally, studies on venous blood gas analysis agree that the former in many, but definitely not all, settings can replace ABG analysis. Exploring these different settings could be of interest since venous sampling is executed in many patients anyway and is said to be more convenient: arterial sampling is not always possible, for instance in early stages of resuscitation \[31–38\]. Moreover, we advise APs to be performed following protocol: work as clean as possible, use the correct equipment and keep the indications and contraindications in mind, such as described by Dev et al. (2011) \[39\].

**Strengths and limitations**

No other study of this size on APs and subsequent complications has ever been undertaken; data were collected in multiple settings over a period of 20 years. The CPR-registry allowed complete follow-up for all patients with a Danish CPR-number. The sample size provided unique evidence about major complications and the rate at which they occur. If there was a clinically significant major complication, it would have been registered. All of these components contribute to the high external validity of our results.

Unfortunately, there are limitations to this historical cohort study. By excluding patients with APs ordered by the anaesthesiology department or ICU, it can be assumed that a healthier patient population was sampled. Since this is a register-based study, only complications that were actually registered could be included; perhaps patients had a major complication after discharge and did not return to the hospital. While we knew that APs have minor complications, using the current set-up, we could not analyse this, as complications not requiring procedures would not be obtainable in the registers. Moreover, it is not clear whether APs and complications were related: we only described the registration of procedures and diagnoses (i.e. a proxy of a major complication) which we assumed were the result of an AP. Possibly complications were registered with multiple codes: one complication could have been followed by several procedures. In that case our analysis made the assumption that one patient had more than one complication, thus leading to an overestimation of the realistic complication rate. Perhaps the way SKS and ICD codes were used and registered could contribute to the reduction in incidence of major complications during the study period. Unfortunately, due to the descriptive and observational nature of this study design, no causal relationship can be described. The chosen cut-off point was 7 days after the AP; if a major complication occurred later, we assumed that the cause was not related to the AP. Naturally it is possible that some of the major complications presented themselves outside our chosen 7-day time-frame; this

**TABLE 7** Unmatched logistic regression on patients with and without complications

| Covariate                              | Unadjusted odds ratio (95% CI) | Adjusted odds ratio (95% CI) |
|----------------------------------------|-------------------------------|-----------------------------|
| **Sex**                                |                               |                             |
| Female                                 | Ref.                          |                             |
| Male                                   | 1.41 (1.20–1.64)              |                             |
| **Age**                                |                               |                             |
| 18–64 years                            | Ref.                          |                             |
| 65–79 years                            | 1.02 (0.86–1.22)              |                             |
| 80+ years                              | 0.87 (0.70–1.10)              |                             |
| **Charlson Comorbidity Index**         |                               |                             |
| 0                                      | Ref.                          |                             |
| 1                                      | 1.12 (0.92–1.37)              |                             |
| 2                                      | 0.78 (0.61–1.00)              |                             |
| ≥3                                     | 0.94 (0.76–1.16)              |                             |
| **Antithrombotic medication use**      |                               |                             |
| No                                     | Ref.                          |                             |
| Yes                                    | 1.26 (1.04–1.54, p=0.02)      | 1.31 (1.07–1.61)            |
| **Arterial puncture in previous 7 days**|                               |                             |
| No                                     | Ref.                          |                             |
| Yes                                    | 0.89 (0.76–1.04)              |                             |

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would not say anything about the 7-day complication rate but could be relevant to the overall presumption of the safety of APs. Furthermore, as ICD codes are registered at discharge or at the time of in-hospital transfer, possibly patients with a longer length of stay – presumably the sicker patient population – with a major complication were missed due to the 7-day cut-off point. Also, major complications were subjectively defined; various specialists assessed them with different opinions on what was considered to be a major complication and how likely it was to occur. Owing to agreement by oral consensus by the two clinicians, it was not possible to calculate a Kappa value. If physicians from other specialities performed assessment, it is plausible that the major complication rates could have differed.

Conclusion

APs for ABG analysis are safe. We found the 7-day major complication rate to be 0.14% (95% CI 0.13–0.15). The complications recorded were embolisms or thrombosis (49.0%), aneurysms (15.4%), nerve damage (1.5%), arteriovenous fistulas (0.6%) or of another kind (33.5%). Patients who have fulfilled an antithrombotic drug prescription within 90 days before the AP have an increased risk of developing major complications.

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