Early View

Original research article

Arterial Blood Gas Analysis: as safe as we think? A multicentre historical cohort study

Sacha C Rowling, Marianne Fløjstrup, Daniel Pilsgaard Henriksen, Bjarke Viberg, Christian Hallenberg, Jes Sanddal Lindholt, Andreas Alberg-Fløjborg, Prabath WB Nanayakkara, Mikkel Brabrand

Please cite this article as: Rowling SC, Fløjstrup M, Henriksen DP, *et al.* Arterial Blood Gas Analysis: as safe as we think? A multicentre historical cohort study. *ERJ Open Res* 2022; in press (https://doi.org/10.1183/23120541.00535-2021).

This manuscript has recently been accepted for publication in the *ERJ Open Research*. It is published here in its accepted form prior to copyediting and typesetting by our production team. After these production processes are complete and the authors have approved the resulting proofs, the article will move to the latest issue of the ERJOR online.

Copyright ©The authors 2022. This version is distributed under the terms of the Creative Commons Attribution Non-Commercial Licence 4.0. For commercial reproduction rights and permissions contact permissions@ersnet.org

Arterial Blood Gas Analysis: as safe as we think? A multicentre historical cohort study

Sacha C Rowling (0000-0003-3531-5275) ^{1,2}, Marianne Fløjstrup (000-0003-3023-1638) ¹⁴, Daniel Pilsgaard Henriksen (0000-0003-1303-6195) ¹, Bjarke Viberg (0000-0001-5169-4282) ³, Christian Hallenberg (0000-0002-9518-8346) ³, Jes Sanddal Lindholt 0000-0001-9536-4488) ¹, Andreas Alberg-Fløjborg (0000-0001-8333-2585) ⁴, Prabath WB Nanayakkara (0000-0002-1555-3682) ², Mikkel Brabrand (0000-0002-3340-8251) ^{1,4}

¹Odense University Hospital, University of Southern Denmark, ²Amsterdam University Medical Center, Location VU university medical centre, Vrije Universiteit Amsterdam, ³Hospital Lillebaelt - University Hospital of South West Jutland, Esbjerg, Denmark

Corresponding author: Sacha C Rowling

sacharowling@live.nl

Take-home message

Arterial punctures for arterial blood gas analysis are safe procedures with a major complication rate within seven days of 0.14% (CI 0.13-0.15). Patients on antithrombotic medication have an increased risk of developing major complications.

Declarations

Funding sources

The authors declare to have received no external funding for this project.

Conflicts of interest

The authors declare that they have no conflict of interest.

Availability of data and material

The corresponding author can be contacted about information on how to access any supplemental information such as the study protocol, raw data or programming code but raw data cannot be exported due to Danish law.

Authors' contributions

Andreas Alberg-Fløjborg, Marianne Fløjstrup and Daniel Pilsgaard Henriksen contributed substantially to the process of data analysis. Daniel Pilsgaard Henriksen, Bjarke Viberg, Christian Hallenberg, Jes Sanddal Lindholt and Mikkel Brabrand assessed and selected the major complications as described in the methods section. Prabath WB Nanayakkara and Mikkel Brabrand gave supervision throughout the entire study. All of the authors critically revised the work and gave their final approval of the version to be published.

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 seven days after puncture and investigating whether using antithrombotic medication affected this.

Methods: We included all APs performed for ABG analysis at three Danish hospitals from 1 January 1993 until 25 February 2013. We excluded APs ordered by the anaesthesiology department, intensive care unit (ICU) or in patients <18 years. Data on patient level was extracted from the Danish National Patient Registry, Danish Civil Registration System and Odense Pharmaco-Epidemiologic Database (OPED), the latter providing us with information on antithrombotics 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%, 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, CI 1.07 - 1.61)).

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

Keywords: arterial puncture, blood gas analysis, complications, blood sampling, antithrombotic

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 outdated studies that mainly focus on minor complications. For example, 4342 arterial punctures obtained in a military setting from 1969 to 1970 resulted in a number of 25 hematomas (0.58%), none defined as a major complication [8]. A study using CT scans revealed hematoma formation in 128 out of 270 patients (47.4%), none of these 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 paraesthesia, to hematoma formation. Again, none of the complications were to be considered as major [10]. All the previously found minor complications resolved spontaneously [8-10]. Major complications have generally been defined as leading to prolonged hospitalization time or a need for surgical treatment or another intervention due to ischemia or other objective abnormalities [8-12]. Described major complications include thrombosis with distal ischemia, major haemorrhages and hematomas, (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 ischemia 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 do 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: it is a routinely performed procedure and the consequences 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 proportion of major complications, seven days after APs for ABG analyses. Our secondary aim is to analyse whether patients on antithrombotic medication prior to hospitalization have a higher complication rate. Our hypothesis is that there is a very low major complication rate within seven 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 2008-58-0035) 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 was analysed retrospectively.

Setting

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

Participants

All adult patients (\geq 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 seven 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 = 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 seven days after the AP, which were defined as a procedure or diagnosis registered in the national registries with respectively SKS- or 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 hospitalizations 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 -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 hospitalization was

received from the Odense Pharmaco-Epidemiologic Database (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 (MB and DPH) – 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 (BV) and two vascular surgeons (CH and JSL) – 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 in the Appendix for the list of all the SKS, ICD-8 and -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 in the Appendix.

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 was not with a normal distribution. The effect of sex, age, use of antithrombotic medication, CCI and number of prior APs were examined in an unmatched logistic regression and shown with adjusted and unadjusted odds ratios (OR). If information on the CCI was missing, we assumed that the patient did not have any relevant co-morbidity. We counted the number of APs in the seven 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 was 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 1st of January 1993 until 25th of February 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 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% (CI 0.13-0.15). The complications occurred in 303 patients (0.28%, 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 APs per year from 1993 to 2012 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.

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% (CI 0.12-0.15) in APs in patients without antithrombotic medication use and 0.17% (CI 0.14-0.21) in APs in patients with antithrombotic medication use. We found a statistically significant difference in complication rates in APs in patients on and off antithrombotic medication (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 \geq two 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, CI 1.20-1.64) and using antithrombotic medication (OR 1.31, 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.

Maximum complication rate

From the 473,327 analysed APs, 1762 APs (0.37%, 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%, 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% (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 antithrombotic medication are associated with an increased risk of developing major complications (0.17%, 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 do 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 antithrombotic therapy 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, catheterization and arteriotomy [12]. Concerning the difference in risk related to gender, no similar bibliographic records have been found. Ishii et al. (2012) found no significant difference between complications in male and female, no other studies reported on this outcome variable [9]. This study does not provide an answer to the question why the male sex is associated with an increased complication rate. Moreover, the finding that in the period 1993-4 more complications were recorded in woman was probably due to statistical variation. Our study provides evidence that the number of APs performed in the prior seven days does not increase the adjusted OR on developing a major complication (OR 0.89, 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 setup 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, labeled as complications. Moreover, as we did not 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 utilization 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 utilization 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 contra-indications 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 was 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 sure if APs and complications were actually 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 be of influence on 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 seven 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 seven-day time-frame: this would not say anything about the seven-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 seven-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. Due 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 seven-day major complication rate to be 0.14% (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.

Acknowledgements

The authors express their sincere gratitude to Niels Ibsgaard Agerbek from the Center for Clinical Epidemiology and Research Unit of Clinical Epidemiology at the Odense University Hospital, for all the help in constructing the database.

Table 3 Baseline characteristics of patients having an ABG drawn in the period of 1 January 1993 and 25 February 2013

	Total punctures	Age 18-64 years	Age 65-79 years	Age 80+ years
Total	(n = 473,327)	(n = 177,978)	(n = 205, 228)	(n = 90,121)
Age, median (IQR)	69 (58-77)	53 (43-60)	72 (69-76)	84 (81-87)
Sex				
Male	242,867 (51.3%)	95,811 (53.8%)	104,995 (51.2%)	42,061 (46.7%)
Female	230,460 (48.7%)	82,167 (46.2%)	100,233 (48.8%)	48,060 (53.3%)
Charlson Comorbidity Index (CCI)				
CCI score = 0	134,514 (28.4%)	74,310 (41.8%)	40,733 (19.8%)	19,471 (21.6%)
CCI score = 1	126,142 (26.7%)	45,325 (25.5%)	58,337 (28.4%)	22,480 (24.9%)
CCI score = 2	87,244 (18.4%)	24,101 (13.5%)	43,246 (21.1%)	19,897 (22.1%)
CCI score >3	125,427 (26.5%)	50,449 (17.3%)	83,863 (26.4%)	30,586 (30.5%)

Table 4 Baseline characteristics of patients with a major complication after a puncture for an arterial blood gas was performed in the period of 1 January 1993 and 25 February 2013

	Total punctures	Age 18-64 years	Age 65-79 years	Age 80+ years
Total	(n = 669)	(n = 255)	(n = 300)	(n = 114)
Age, median (IQR)	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				
(CCI)				
CCI score = 0	192 (28.7%)	71 (27.8%)	92 (30.7%)	29 (25.4%)
CCI score = 1	201 (30.0%)	95 (37.3%)	91 (30.3%)	15 (13.2%)
CCI score = 2	99 (14.8%)	40 (15.7%)	34 (11.3%)	25 (21.9%)
CCI score >3	177 (26.5%)	49 (19.2%)	83 (27.7%)	45 (39.5%)
	, ,	,	• ,	, ,

Table 5 Major complications after an arterial puncture for arterial blood gas analysis

	Total complications	% of total complications
Total	(n = 669)	(100.0%, CI)
Embolisms or thrombosis	328	49.0% (45.2 – 52.9)
Aneurysms	103	15.4% (12.7 – 18.4)
Nerve damage	10	1.5% (0.72 – 2.7)
Arteriovenous fistulas	4	0.6% (0.16 – 1.5)
Other	224	33.5% (29.9 – 37.2)

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 (%, CI)	Complications (%, CI)	P-value
Total	(n = 472,658, 100%)	(<i>n</i> = 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	9,776 (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

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 (CCI)		
CCI score = 0		Ref.
CCI score = 1		1.12 (0.92-1.37)
CCI score = 2		0.78 (0.61-1.00)
CCI score >3		0.94 (0.76-1.16)
Antithrombotic medication use		
No	Ref.	Ref.
Yes	1.26 (1.04-1.54, p=0.02)	1.31 (1.07-1.61)
Arterial puncture in previous seven days		0.89 (0.76-1.04)

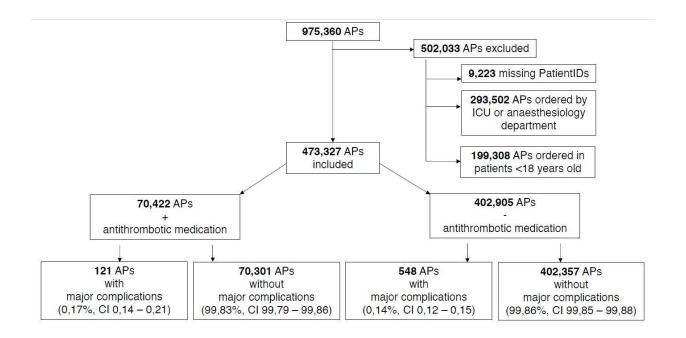


Fig. 1 Flowchart of major complications in arterial punctures in patients on and off antithrombotic medication, in three hospitals in Denmark from 1993 to 2012

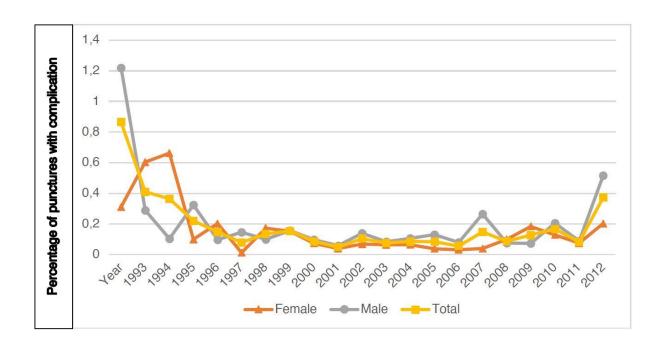


Fig. 2 Percentage of arterial punctures leading to a major complication, stratified by sex and year in three hospitals in Denmark from 1993 to 2012

References

- Melanson, S. E. F., Szymanski, T., Rogers, S. O., Jarolim, P., Frendl, G., Rawn, J. D., Ferrigno, M.
 (2007). Utilization of arterial blood gas measurements in a large tertiary care hospital. *American Journal of Clinical Pathology*, 127(4), 604–609. https://doi.org/10.1309/ELH5BPQ0T17RRK0M
- Sado, D. M., Bsc, B., Deakin, C. D., & Frca, M. (2005). Local anaesthesia for venous cannulation and arterial blood gas sampling: are doctors using it? *J R Soc Med*, *98*(32), 158–160.
 https://doi.org/10.1258/jrsm.98.4.158
- 3. Giner, J., Casan, P., Belda, J., González, M., Ma Miralda, R., & Sanchis, J. (1996). Pain during arterial puncture. *Chest*, *110*(6), 1443–1445. https://doi.org/10.1378/chest.110.6.1443
- 4. Hajiseyedjavady, H., Saeedi, M., Eslami, V., Shahsavarinia, K., & Farahmand, S. (2012). Less painful arterial blood gas sampling using jet injection of 2% lidocaine: A randomized controlled clinical trial. *American Journal of Emergency Medicine*, 30(7), 1100–1104. https://doi.org/10.1016/j.ajem.2011.07.011
- Turner, J. S., Briggs, S. J., Springhorn, H. E., & Potgieter, P. D. (1990). Patients' recollection of intensive care unit experience. *Critical Care Medicine*, 18(9), 966-968.
 https://doi.org/10.1097/00003246-199009000-00012
- 6. Roberts, J. R., Custalow, C. B., Thomsen, T. W., & Hedges, J. R. (2014). Arterial Puncture and Cannulation. In H. T. Kim (Ed.), *Roberts and Hedges' clinical procedures in emergency medicine* (pp.368-384). Philadelphia, Pennsylvania: Saunders, an imprint of Elsevier Inc.
- Walensi, M., & Elsner, A. (2016). Arterieller Zugang–Indikationen, Techniken,
 Komplikationen. Deutsche Medizinische Wochenschrift, 141(22), 1630-1635. doi: 10.1055/s-0042-115389
- 8. Fleming, W. H., & Bowen, J. C. (1974). Complications of arterial puncture. *Military medicine*, 139(4), 307-308.

- Ishii, S., Miyajima, M., Shishido, F., & Sakuma, K. (2012). Hematoma After Femoral Arterial Blood Sampling. *Journal of Computer Assisted Tomography*, 36(2), 257–260. https://doi.org/10.1097/RCT.0b013e3182483c55
- 10. Okeson, G. C., & Wulbrecht, P. H. (1998). The Safety of Brachial Artery Puncture for Arterial Blood Sampling *. *Chest*, *114*(3), 748-751. https://doi.org/10.1378/chest.114.3.748
- 11. Tong, Z., Gu, Y., Guo, L., Guo, J., Gao, X., Li, J., ... & Zhang, J. (2016). An Analysis of Complications of Brachial and Axillary Artery Punctures. *The American Surgeon, 82*(12), 1250-1256.
- 12. Mortensen, J. D. (1967). Clinical sequelae from arterial needle puncture, cannulation, and incision. *Circulation*, *35*(6), 1118–23. https://doi.org/10.1161/01.CIR.35.6.1118
- 13. Ara, C., Coban, S., Isik, B., Ozcan, C. C., & Yilmaz, S. (2010). Small bowel perforation after drawing a blood sample in the femoral artery: a case report. *Ulus Travma Acil Cerrahi Derg, 16*(3), 275–276. Retrieved from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=20517757
- 14. Criscuolo, C., Nepper, G., & Buchalter, S. (1995). Reflex Sympathetic Dystrophy Following

 Arterial Blood Gas Sampling in the Intensive Care Setting. *Chest*, *108*(2), 578–580.

 https://doi.org/10.1378/chest.108.2.578
- 15. Marshall, G., Edelstein, G., & Hirshman, C. A. (1980). Median nerve compression following radial arterial puncture. *Anesthesia and Analgesia*, *59*(12), 953–954. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed1a&AN=19
 https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed1a&AN=19
 <a href="https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emed1a&AN=19
 <a href="https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=JC&CSC=JC&DA

- Matsagas, M. I., Mitsis, M., Rigopoulos, C., Theodossiou, V., Koulouras, V., Polyzoidis, K., & Kappas, A. M. (2003). A large radial artery false aneurysm after repeated arterial punctures, causing compartment syndrome of the forearm. *Intensive Care Medicine*, 29(6), 1032. https://doi.org/10.1007/s00134-003-1762-7
- 17. Matthews, J. I., & Gibbons, R. B. (1971). Embolization complicating radial artery puncture. *Ann Intern Med, 75*(1), 87-88.
- 18. Patel, K. N., Gandhi, S. P., & Sutariya, H. C. (2016). Radial artery pseudoaneurysm: A rare complication after a single arterial puncture for blood-gas analysis. *Indian Journal of Critical Care Medicine*, 20(10), 622–627. https://doi.org/10.4103/0972-5229.192066
- 19. Russo, G., Cherubini, A., Fisicaro, M., Cioffi, G., & Di Lenarda, A. (2016). Radial pseudoaneurysm after a puncture for blood gas analysis. *American Journal of Emergency Medicine*, *34*(4), 757.e1-757.e2. https://doi.org/10.1016/j.ajem.2015.07.064
- 20. Malík, J., Holaj, R., Krupičková, Z., & Janota, T. (2012). Arteriovenous fistula after femoral artery puncture leading to pulmonary edema: the role of ultrasonography. *Prague medical report*, 113(1), 49-52.
- 21. Berger, A. (1989). Brachial artery puncture: the need for caution. *Journal of Family Practice,* 28(6), 720-722.
- 22. Neviaser, R. J., Adams, J. P., & May, G. I. (1976). Complications of arterial puncture in anticoagulated patients. *JBJS*, *58*(2), 218-220
- 23. Benchimol, E. I., Smeeth, L., Guttmann, A., Harron, K., Moher, D., Petersen, I., ... & RECORD Working Committee. (2015). The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. *PLoS medicine*, *12*(10), e1001885.
- 24. Quan, H., Li, B., Couris, C. M., Fushimi, K., Graham, P., Hider, P., ... & Sundararajan, V. (2011).

 Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital

- discharge abstracts using data from 6 countries. *American journal of epidemiology, 173*(6), 676-682. https://doi.org/10.1093/aje/kwq433
- 25. Radovanovic, D., Seifert, B., Urban, P., Eberli, F. R., Rickli, H., Bertel, O., ... & AMIS Plus Investigators. (2013). Validity of Charlson Comorbidity Index in patients hospitalised with acute coronary syndrome. Insights from the nationwide AMIS Plus registry 2002–2012. Heart, heartjnl-2013. https://doi.org/10.1136/heartjnl-2013-304588
- 26. Schmidt, M., Pedersen, L., & Sørensen, H. T. (2014). The Danish Civil Registration System as a tool in epidemiology. *European Journal of Epidemiology*, 29(8), 541–549.
 https://doi.org/10.1007/s10654-014-9930-3
- Schmidt, M., Schmidt, S. A. J., Sandegaard, J. L., Ehrenstein, V., Pedersen, L., & Sørensen, H. T.
 (2015). The Danish National patient registry: A review of content, data quality, and research potential. *Clinical Epidemiology*, 7, 449–490. https://doi.org/10.2147/CLEP.S91125
- 28. Bjerrum, L., & Bergman, U. (2000). Wide variation in the number of different drugs prescribed by general practitioners A prescription database study. *Scand J Prim Health Care, 18*(2), 94–98. https://doi.org/10.1080/028134300750018972
- 29. Jarlbaek, L., Andersen, M., Kragstrup, J., & Hallas, J. (2004). Cancer patients' share in a population's use of opioids. A linkage study between a prescription database and the Danish Cancer Registry. *Journal of Pain and Symptom Management, 27*(1), 36–43. https://doi.org/10.1016/j.jpainsymman.2003.05.002
- 30. Gillies, I. D. S., Morgan, M., Sykes, M. K., Brown, A. E. & Jones, N. O. (1979). The nature and incidence of complications of peripheral arterial puncture. *Anaesthesia*, *34*(5), 506-509.
- 31. Brandenburg, M. A, & Dire, D. J. (1998). Comparison of arterial and venous blood gas values in the initial emergency department evaluation of patients with diabetic ketoacidosis. *Ymem,* 31(4), 459–465. https://doi.org/10.1016/S0196-0644(98)70254-9

- 32. Burri, E., Potocki, M., Drexler, B., Schuetz, P., Mebazaa, A., Ahlfeld, U., ... Mueller, C. (2011).

 Value of arterial blood gas analysis in patients with acute dyspnea: An observational study.

 Critical Care, 15(3), R145. https://doi.org/10.1186/cc10268
- 33. Malatesha, G., Singh, N. K., Bharija, A., Rehani, B., & Goel, A. (2007). Comparison of arterial and venous pH, bicarbonate, PCO2 and PO2 in initial emergency department assessment. *Emergency Medicine Journal*, 24(8), 569–571. https://doi.org/10.1136/emj.2007.046979
- 34. Middleton, P., Kelly, A. M., Brown, J., & Robertson, M. (2006). Agreement between arterial and central venous values for pH, bicarbonate, base excess, and lactate. *Emergency Medicine Journal*, 23(8), 622–624. https://doi.org/10.1136/emj.2006.035915
- 35. Kelly, A.-M. (2010). Review article: Can venous blood gas analysis replace arterial in emergency medical care. *Emergency Medicine Australasia*, *22*(6), 493–498. https://doi.org/10.1111/j.1742-6723.2010.01344.x
- Rudkin, S. E., Kahn, C. A., Oman, J. A., Dolich, M. O., Lotfipour, S., Lush, S., ... Langdorf, M. I.
 (2012). Prospective correlation of arterial vs venous blood gas measurements in trauma patients. *American Journal of Emergency Medicine*, 30(8), 1371–1377.
 https://doi.org/10.1016/j.ajem.2011.09.027
- 37. Treger, R., Pirouz, S., Kamangar, N., & Corry, D. (2010). Agreement between Central Venous and Arterial Blood Gas Measurements in the Intensive Care Unit. *Clin J Am Soc Nephrol*, *5*(3), 390–394. https://doi.org/10.2215/cjn.00330109
- 38. Walkey, A. J., Farber, H. W., O'Donnell, C., Cabral, H., Eagan, J. S., & Philippides, G. J. (2010). The accuracy of the central venous blood gas for acid-base monitoring. *Journal of Intensive Care Medicine*, 25(2), 104–110. https://doi.org/10.1177/0885066609356164
- 39. Dev, S. P., Hillmer, M. D., & Ferri, M. (2011). Arterial puncture for blood gas analysis. *N Engl J Med, 364*(5), e7.

Appendices

Table 1 List of SKS, ICD-8 and -10 codes that are possibly related to an arterial puncture, as selected by two clinical physicians and categorised by three independent blinded surgeons

Code	Very likely	Possible but unlikely	Not possible
44299 – Aneurysm arteria aliud	Х		XX
44441 – Embolism, thrombosis arteria femoralis	Х		XX
44442 - Embolism, thrombosis arteria popliteae	Х		XX
44444 - Embolism, thrombosis arteria periphericae			
extremitatis	Х		XX
68229 - Inflammation, abscess and acute			
lymphangioma. brachii and antebrachii	Х		XX
95209 – Traumatic leasion plexus brachialis and nervi			
brachii, uncomplicated	Х		XX
DG560 – Carpal tunnel syndrome		Х	XX
DG562 – Neuropathy in nervus ulnaris			XXX
DI721 – Aneurism upper extremity	ХX		Х
DI721 – Aneurism in artery in upper extremity	Х	Х	Х
DI724 - Aneurism in artery in lower extremity	XX		Х
DI729 - Aneurism unspecified	XX		Х
DI742 – Embolism or thrombosis in artery in upper			
extremity	ХX		X
DI742A - Embolism or thrombosis in upper extremity	Х	Х	Х
DI742A - Emboli arteria brachialis	Х	Х	Х
DI742B - Thrombosis in artery in upper extremity	ХX		Х
DI742B - Thrombosis arteria brachialis	ХX		Х
DI743 - Embolism or thrombosis in artery in lower			
extremity	ХX		X
DI743A - Embolism in artery in lower extremity	Х	Х	Х
DI743B - Thrombosis in artery in lower extremity	ХX		Х
DI744 - Embolism or thrombosis in artery in			
unspecified extremity	Х		XX
DI748 – Embolism or thrombosis in other artery		X	XX
DI749 - Embolism or thrombosis in artery unspecified	Х		XX
DI770 - Acquired A-V fistula	ХX		Х
DI771 – Artery stricture	Х	Х	Х
DI771 – Stricture of artery	Х		XX
DI772 – Artery rupture			XXX
DI775 – Artery necrosis		X	XX
DI803A – Embolism in lower extremity unspecified		X	XX
DM622A – Non-traumatic compartment syndrome			XXX
DS451 – Lesion of arteria brachialis	ХX		Х
DS540 - Lesion of nervus ulnaris in elbow region or			
lower arm		X	XX

DS541 – Lesion of nervus medianus in elbow region			
or lower arm	Х	Χ	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	ХX	Χ	
DS551 – Lesion of arteria radialis in elbow region or			
lower arm	XXX		
DS561 – Lesion of muscle/tendon of long flexor to a			
finger on lower arm		Х	XX
DS562 – Lesion of muscle or tendon of other flexor on			
lower arm		X	XX
DS568 – Lesion of an or unspecified muscle or tendon			
in elbow/lower arm		Χ	XX
DS641 – Lesion of nervus medianus in wrist or hand	X	Χ	X
DS659 – Lesion of blood vessel in wrist or hand			
unspecified	XX		X
DS660 – Lesion of long flexors to thumb in wrist/hand		Χ	XX
DS661 – Lesion of flexors to unspecified finger in wrist			
or hand		Х	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	XX		X
DT802 - Infection after infusion, transfusion or			
injection	XX		X
DT808 – Other complication after infusion,			.,
transfusion or injection	XX		X
DT809 – Complication after infusion, transfusion or	V. V.		
injection unspecified	XX		X
DT812K - Inadverted preoperative puncture/lesion of	V	V	V
vein or lymph system	X	X	X
DT814 – Infection after intervention unspecified		XX	X
DT817 – Complication in vessel after intervention	V	ХX	
unspecified DT817B – Thromboembolic complication unspecified	Х	XX	X
DT817K - Thrombosis, embolism or necrosis after		^ ^	^
vessel operation			xxx
DT819 – Complication of procedure unspecified		Х	XX
DT88 – Complication of procedure dispectified DT88 – Complications with or with surgery	X	X	X
DT888 – Complication with surgery or with	^	^	^
unspecified treatment, other specified	Х	ХX	
KACA11 - Exploration, n. medianus	^	X	XX
KACA11 - Exploration, n. medianus KACA13 - Exploration, n. ulnaris		X	XX
KACC51 - Decompression and loosening of nervus		Λ	
medianus		ХX	x
mediana		ΛΛ	^

KACC53 - Decompression and loosening of nervus		
ulnaris	ХX	X
KNCA00 - Exploration in soft tissue in lower arm,		
percutaneous	X	XX
KNCA02 - Exploration in soft tissue in lower arm,		
open	X	XX
KNCM09 – Fasciotomy in lower arm	XX	Х
KNCM19 – Resection or excision of fasciae in lower		
arm		XXX
KNCM99 – Operation on fasciae, tendons, ganglion,		
bursa, elbow/lower arm, other		XXX
KNCS09 - Incision/revision of infection in tendon in		
elbow/lower arm	X	XX
KNCS99 – Operation for infection in tendons, joints		
and bones, elbow / lower arm, other	X	XX
KNDA02 - Exploration of soft tissue, wrist and hand,		
open	X	XX
KNDM09 - Fasciotomy of wrist/hand		XXX
KNDM19 - Fasciotomy partial/total (incl. op pro mb.		
Dupuytren)	X	XX
KNDS09 - Incision/revision of infection in tendon in		
wrist/hand	X	XX
KNDS99 – Other operation for infection in tendon,		
joint or bone in wrist/hand	X	XX
KQCA00 – Puncture of skin in upper extremity		XXX
KQCA10 - Incision of skin in upper extremity		XXX
KQCA99 - Incision of skin in upper extremity, other		XXX
KQCB00 – Suture of skin in upper extremity		XXX
KQCB05 – Wound revision in upper extremity	Х	XX
KQCB10 – Replacement of larger wounds in upper		
extremity	X	XX
KQCB99 – Wound treatment in upper extremity,		
other	X	XX
KTNC00 – Puncture or needle biopsy in elbow/lower		
arm	X	XX
KTNC05 - Minor incision or soft tissue in elbow/lower		
arm	X	XX
KTND00 – Puncture or needle biopsy in wrist/hand	XX	Х
KTND05 - Minor incision of soft tissue in wrist/hand	Х	XX

Table 2 List of SKS, ICD-8 and -10 codes that were registered in patients that had a complication after an AP, categorised into five categories

Code		Category
DI742	Embolism or thrombosis in artery in upper extremity	Embolism or Thrombosis
DI743	Embolism or thrombosis in artery in lower extremity	Embolism or Thrombosis
DI743A	Embolism in artery in lower extremity	Embolism or Thrombosis
DI743B	Thrombosis in artery in lower extremity	Embolism or Thrombosis
DI744	Embolism or thrombosis in artery in unspecified extremity	Embolism or Thrombosis
DI749	Embolism or thrombosis in artery unspecified	Embolism or Thrombosis
44441	Embolism, thrombosis arteria femoralis	Embolism or Thrombosis
44442	Embolism, thrombosis arteria popliteae	Embolism or Thrombosis
44444	Embolism, thrombosis arteria periphericae extremitatis	Embolism or Thrombosis
DI721	Aneurism upper extremity	Aneurysm
DI721	Aneurism in artery in upper extremity	Aneurysm
DI724	Aneurism in artery in lower extremity	Aneurysm
DI729	Aneurism unspecified	Aneurysm
44299	Aneurysm arteria aliud	Aneurysm
DS541	Lesion of nervus medianus in elbow region or lower arm	Nerve damage
DS641	Lesion of nervus medianus in wrist or hand	Nerve damage
DI770	Acquired A-V fistula	Arteriovenous fistulas
DS550	Lesion of nervus ulnaris in elbow region or lower arm	Other
DS750	Lesion in arteria femoralis	Other
DT145	Lesion in blood vessel without indication of body region	Other
DT801	Complication in vessel after infusion, transfusion on injection	Other
DT808	Other complication after infusion, transfusion or injection	Other
DT809	Complication after infusion, transfusion or injection unspecified	Other
DT812K	Inadverted preoperative puncture/lesion of vein or lymph system	Other
DT817	Complication in vessel after intervention unspecified	Other
DT88	Complications with or with surgery	Other
DT888	Complication with surgery or with unspecified treatment, other specified	Other
68229	Inflammation, abscess and acute lymphangioma. brachii and antebrachii	Other