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Original paper

Success rate of adrenal venous sampling and predictors for success: a retrospective study

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Abstract

Purpose: To report the success rate of adrenal venous sampling (AVS) and identify the predictors for procedural success.

Material and methods: Sixty-four patients (18 men and 46 women) with a mean ± SD age of 50 ± 11.8 years (range 28-69 years) diagnosed as primary hyperaldosteronism, and who underwent AVS from January 2009 to December 2016, were retrospectively reviewed. In our institution, the initial period to perform the AVS was set from 2009 to 2013, and the post-initial period was defined as procedures performed after 2013. Successful sampling was determined when the ratio of cortisol from the adrenal vein to the level of cortisol in the inferior vena cava ≥ 5. The procedural success and subject factors between success and failure were analysed. A p value < 0.05 was considered statistically significant.

Results: The success rate of bilateral AVS was 71.9%. The success rates of right and left AVS were 76.6% and 90.6%, respectively. Male patients were more likely to succeed than female patients (adjusted odds ratio [aOR], 9.83; 95% confidence interval [CI], 1.14-85.14; p = 0.009). In our institution, the procedure performed in the post-initial period also succeeded more often compared to the initial period (aOR, 5.05; 95% CI, 1.2-21.16; p = 0.017). No other factors were associated with the success rate in this study.

Conclusions: The success rate of bilateral AVS in our institution was rather high. Male gender and procedure performed in the post-initial period were significant predictive factors for a successful procedure.

Key words: primary aldosteronism, adrenal venous sampling, success, predictive factor.

Introduction

Primary aldosteronism (PA) affects more than 10% [1-3] of all hypertensive patients, of which the two main causes are unilateral aldosterone-producing adenoma (APA) and bilateral adrenal hyperplasia (BAH) [2-5]. Distinguishing the two diagnoses is critical because APA is curable by resection while BAH is treated with medication [1,2,4,5]. Computed tomography (CT) and magnetic resonance image (MRI) are the preferred modalities to detect adrenal adenoma. However, they only help for detection and anatomical diagnosis but cannot determine the biological differentiation between APA and BAH [6].

Adrenal venous sampling (AVS) is the gold standard to diagnose APA and BAH using the ratio of plasma aldosterone to cortical levels between both sides [6-9]. However, AVS is an invasive and difficult procedure even in experienced hands [1,7,8]. A previous publication reported variable success rates of the procedure ranging from 42% to 98% [4-6,10], while complications included groin haematoma, venous thrombosis, venous transection, adrenal haemorrhage, adrenal insufficiency, and hypertensive

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crisis [6,8,11]. Catheterisation into the right adrenal vein is the main difficulty because of the anatomical factors, which include small diameter, short length, and direct drainage into the inferior vena cava (IVC). In contrast, blood sampling from the left adrenal vein is relatively easy due to consistent anatomy. Previous publications reported success rates of right and left blood samplings of 40-94% and more than 90%, respectively [6,8,12-15].

As mentioned, AVS is the gold standard procedure to determine the cause of PA; however, the success rate of the procedure varies. Also, the success rate of the procedure should be a factor in considering the benefits of the investigation. However, there are few data that report the factors of determining success. The objective of this study was to report the success rates of AVS in our hospital and identify the predictors of procedural success.

Material and methods

Patients

This was a retrospective study of all patients who were diagnosed with PA by saline-loading testing or fludrocortisone challenge testing and underwent AVS from January 2009 to December 2016 in Songklanagarind Hospital, which is a university hospital in southern Thailand. Sixty-seven patients who met the inclusion criteria included those diagnosed with PA by clinical and laboratory data as well as the presence of nodules on CT scan or MRI. However, three patients declined the procedure and were excluded. Consequently, the study population included 64 patients. The present study was approved by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University (IRB No. 58-243-07-4).

Procedure

The intravenous infusion consisted of cosyntropin (Synacthen®, Novartis Pharmaceuticals, Dorval, Québec, Canada) 0.25 mg in 500 ml of 5% dextrose in water infused at 100 ml/h for at least 30 minutes before the AVS. The procedure was performed by standard percutaneous transfemoral vein catheterisation using a 5-French (Fr) sheath under local anaesthesia. A 5-Fr angiographic catheter using a Cobra with one side-hole (Terumo Europe, Leuven, Belgium) was used for catheterisation into the right adrenal vein and a Simon II (Boston Scientific, MA, USA) for catheterisation into the left adrenal vein. A 6 ml sample of blood was taken from each adrenal vein, and 10 ml of blood was sampled from the IVC. The sample evaluated the cortisol ratio to confirm successful catheterisation. Haemostasis at the puncture site was assured by manual compression. In our hospital, AVS was performed by fluoroscopic guidance by digital subtraction angiography (INTEGRIS V5000; Philips, Best, The Netherlands) from 2009 to 2013 (initial period). Additionally, there were four

interventional radiologists performing AVS during the initial period. After 2013 (post-initial period), AVS was performed by single-plane digital subtraction angiography (Allura Xper FD; Philips, Best, The Netherlands). However, AVS in this period was performed by a single interventional radiologist who specialised in venous intervention.

Data collection

The data were retrieved from the Radiology Department records and the hospital database. The collected data included the patients' demographic data and technical factors including time of operation, number of correct blood samplings, route of access, and the initial and post-initial periods to perform the procedure.

Definitions

The final success of AVS was defined as a ratio of ≥ 5 (selectivity index) of the levels of cortisol from each of the left and right adrenal veins to the level of cortisol from the IVC. Failure of the procedure was defined as a selectivity index < 5 from one or two sides. In the cases where blood samples could not be collected from one or both adrenal veins, this was also defined as procedural failure. We also analysed the success of each AVS to determine the outcome.

Statistical analysis

Continuous demographic and technical data are presented as mean ± standard deviation (SD) and range. Categorical data are presented by frequency and percentage. Continuous data of predictive factors for success are represented by Student's t-test and Wilcoxon rank sum test, and the categorical data of predictors for success were calculated by χ^2 and Fisher's exact tests. The significant predictive factors from univariate analysis were also calculated by multivariate logistic regression. A p value less than 0.05 was considered statistically significant.

Results

This study included 64 patients who underwent AVS in our hospital. The number of AVS procedures in this centre was seven to nine procedures per year. The demographic and technical data are shown in Table 1. Our subjects were predominately female (46 patients). The mean age ± SD was 50 ± 11.8 years, and the mean BMI ± SD was 25.8 ± 5.1 kg/m². The mean ± SD systolic and diastolic blood pressures were 148 ± 21 mmHg and 89 ± 13 mmHg, respectively. Most patients had nodules (48.4%) on the left adrenal gland. AVS was performed mostly via the right common femoral vein approach (90.6%).

The success rates are presented in Table 2. The success rates of right and left blood samplings were 76.6% and

90.6%, respectively. The final success rate of the procedure was 71.9%. Failure of procedure was found in three patients. Failure to collect blood from the right adrenal vein with a left selectivity index of < 5 was found in two patients. Another case had a selectivity index < 5 from both sides. The success rates of right and left adrenal blood samplings in male vs. female were 94.4% vs. 69.9% ($p = 0.048$) and 100% vs. 87% ($p = 0.173$), respectively. The success of right and left adrenal samplings performed in the initial five-year and post-initial three-year periods were 67.6% vs. 88.9% ($p = 0.091$) and 83.8% vs. 100% ($p = 0.035$), respectively. The details of success of procedure are shown in Table 3. Univariate analysis was used to identify factors affecting the success of the procedure. The results showed statistical significance of two factors that included gender ($p = 0.005$) and the period of procedure ($p = 0.007$).

The significant predictive factors are shown in Table 4. By multivariate logistic analysis, the gender and the period of procedure were confirmed to be significant factors associated with success. Success of the procedure in male patients was about 10 times greater than in female patients (adjusted odds ratio [aOR], 9.83; 95% confidence interval [CI], 1.14-85.14; $p = 0.009$). Success of the procedure performed in the post-initial period in our institute was five times greater than in the initial period (aOR, 5.05; 95% CI, 1.2-21.16; $p = 0.017$).

Discussion

In the current study, the final success rate of AVS was in the range of success rates from previous reports [4-6,10]. When an evaluation of the success rates was performed for each side, we found the success rate of blood sampling from the left side was higher than from the right side. Gender and the period of the procedure were the only two significant predictive factors of success associated with the high odds ratios in this study. The other variables were not significant factors to determine success.

The final success rate in this study was 71.9%, which was rather high compared to previous studies [4-6,10] because of the influence of the result of the initial first five experiences (2009-2013), showing a 59% success rate. Additionally, our centre is a low-volume centre, which performs less than 20 AVS procedures per year. However, the success rate increased to 89% in the post-initial three-year period (2014-2016). Similar results were reported by Jakobsson *et al*. [14] and Siracuse *et al*. [16], who showed increased success rates after their initial period from 38% to 92% and from 58% to 82%, respectively. Better outcomes were due to the gains in experience and skill.

The success rates of the right and left AVS in this study were 76.6% and 90.6%, respectively. The success rate of the right AVS was reported to range from 81% to 97% in experienced interventionists, while the success rates were 40% to 80% in low-volume centres or from less

Table 1. Patients' demographic data and technical parameters

Parameters	n (%)
Patients	
Age (mean 50 ± 11.8 years; range 28-69 years)	
Gender	
Male	18 (28.1)
Female	46 (71.9)
Height (mean, 1.6 ± 1.0 m; range 1.45-1.80 m)	
Weight (mean, 64.8 ± 15.2 kg; 40.5-85 kg)	
BMI (mean 25.8 ± 5.1 kg/m²)	
< 23	32 (50)
≥ 23	32 (50)
Systolic BP (mean, 147.9 ± 21.1 mmHg; range 110-230 mmHg)	
Diastolic BP (mean, 89 ± 13 mmHg; range 52-114 mmHg)	
Aldosterone (mean, 78.6 ± 48.4 ng/dl; range 11-307 ng/dl)	
Potassium (mean, 3 ± 0.7 mEq/l; range 1.9-4.9 mEq/l)	
Adrenal nodule (side)	
None	2 (3.1)
Right side	28 (43.8)
Left side	31 (48.4)
Both sides	3 (4.7)
Visibility of right adrenal vein	
Present on CT/MRI	60 (93.7)
Non-present on CT/MRI	4 (6.3)
Technique	
Time of procedure	
Morning	39 (60.9)
Afternoon	25 (39.1)
Route of access	
Right common femoral vein	58 (90.6)
Left common femoral vein	5 (7.8)
Both common femoral veins	1 (1.6)
Number of right blood samplings per procedure	
One	36 (56.3)
Two	26 (40.6)
No sampling	2 (3.1)
Period of procedure	
2009-2013	37 (57.8)
2014-2016	27 (42.2)

BMI – body mass index, BP – blood pressure, CT – computed tomography, MRI – magnetic resonance imaging

Table 2. Success rates of adrenal venous sampling

Adrenal venous sampling	Right n (%)	Left n (%)	Bilateral n (%)
Success	49 (76.6)	58 (90.6)	46 (71.9)
Failure	15 (23.4)	6 (9.4)	18 (28.1)

Table 3. Univariate analysis for success of blood sampling ($n = 64$)

Factors	Right AVS			Left AVS			Both AVS		
	Success $n = 49$	Failure $n = 15$	*p*	Success $n = 58$	Failure $n = 6$	*p*	Success $n = 46$	Failure $n = 18$	*p*
Patients									
Age (year), mean (±SD)	49.8 (11.1)	50.7 (14.4)	0.805	50 (11.9)	50.2 (12.3)	0.971	49.4 (11.1)	51.4 (13.6)	0.545
Gender									
Male	17	1	0.048*	18	0	0.173	17	1	0.005*
Female	32	14		40	6		29	17	
Height (m), mean (±SD)	1.6 (0.1)	1.6 (0.1)	0.383	1.6 (0.1)	1.6 (0)	0.732	1.6 (0.1)	1.6 (0.1)	0.265
Weight (kg); median (IQR)	66 (54.7, 74.8)	61.6 (51.5, 66.3)	0.506	65.9 (54.2, 74.3)	56.2 (52.3, 60)	0.167	66 (55, 75)	59 (51.4, 65.5)	0.196
BMI (kg/m^2)									
< 23	23	9	0.555	27	5	0.196	20	12	0.164
≥ 23	26	6		31	1		26	6	
Technique									
Right adrenal vein level from selection									
T11	11	3	1.000	–	–	–	11	3	0.975
T12	25	6		–	–		23	8	
L1	13	4		–	–		12	5	
Time of procedure									
Morning	31	8	0.698	35	4	1	29	10	0.582
Afternoon	18	7		23	2		17	8	
Route of access									
Right CFV	44	14	1	53	5	0.115	42	16	0.264
Left CFV	4	1		5	0		4	1	
Both CFVs	1	0		0	1		0	1	
Number of right blood samplings per procedure									
One	30	6	0.249	–	–	–	28	8	0.237
Two	19	7		–			18	8	
Period of procedure									
2009-2103	25	12	0.091	31	6	0.035*	22	15	0.007*
2014-2016	24	3		27	0		24	3	

*$p < 0.05$; AVS – adrenal venous sampling, SD – standard deviation, IQR – interquartile range, BMI – body mass index, CFV – common femoral vein

Table 4. Multivariate logistic regression for factors of success of bilateral blood samplings

Factors	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)	*P*
Gender			
Female	1	1	0.009*
Male	9.97 (1.22-81.68)	9.83 (1.14-85.14)	
BMI			
< 23	1	1	0.297
≥ 23	2.6 (0.83-8.13)	1.95 (0.55-6.88)	
Period of procedure			
2009-2013	1	1	0.017*
2014-2016	5.45 (1.39-21.42)	5.05 (1.2-21.16)	

*$p < 0.05$; CI – confidence interval, BMI – body mass index

experienced interventionists [9,17-19]. Previous studies and this current study had similar results, which showed that the success rate of right AVS was lower than for left AVS, and the failure rate of right AVS was about 30% [4-6, 8-10,12,20]. The reason for this is the anatomical difficulty of catheterisation of the right adrenal vein due to its small calibre and short length. A cadaveric study confirmed that the diameters of the right and left adrenal veins were 3.5 mm and 4.5 mm and the mean lengths of the right and left adrenal veins were 7.0 mm and 16.0 mm, respectively [21]. Additionally, the right adrenal vein drains directly into the IVC and has more anatomical variations that lead to a difficult catheterisation.

Gender was the factor associated with success of AVS in this study. AVS performed in males was about ten times

more likely to succeed than in females. The possible reason for this is that the calibre of the adrenal vein in males is larger than in females, which leads to easier catheterisation compared with females. However, from the literature review, there were no data or comparisons between the diameters of the adrenal veins in males and females. One study by Berney *et al.* [22] reported that male gender might significantly influence the success rate of AVS from a univariate analysis. However, there was no significance from the multivariate analysis.

The period of the procedure was also a significant factor associated with success. The procedure performed in the post-initial three-year period was five times more successful than in the initial five-year period in this study. This result was from systematic changes after the initial period, which included a change to a higher quality machine with large flat-panel displays and high-resolution images. Furthermore, the AVS procedure in the post-initial three-year period was performed by a single interventional radiologist who specialised in venous intervention. Similar results from previous studies [7,17,23] suggested that limiting the AVS procedures to a few interventionists increased the success rate. Therefore, this should be the practice in a low-volume centre.

The study by Berney *et al.* [22] also showed that body mass index (BMI) was a significant factor associated with success. An increased BMI may increase the intra-abdominal pressure, leading to a decreased adrenal vein flow, which results in an increased calibre of the adrenal vein, which in turn leads to an easier catheterisation. The average BMI in their study was 29 ± 5.6 kg/m² and a BMI near or more than 30 resulted in an increased success rate. However, BMI was not a factor in our study because the mean $\pm$ SD of the BMI was 25.8 ± 5.1 kg/m². The other factors that included age, level of right adrenal vein selec-tion, time of the procedure, route of access, and the number of right blood samplings per operation were not found to be significant in the current study. Similarly, these factors were not reported to be significant in the literature.

A strength of this study is the evaluation of patient characteristics as predictors of success in AVS, which were not well determined in previous studies. There were some limitations in this study. This study was of retrospective design and was performed at a single centre. However, to improve the impact of the study, a prospective design with a multicentre approach should be performed. Another limitation is the small sample sizes in each group of parameters to compare success and failure. However, we improved the results by using univariate analysis and multivariate logistic regression.

In conclusion, the success rate of bilateral AVS in our study was rather high. However, a high success rate of the procedure in a low-volume centre can occur when performed by a few interventionists. Male gender and post-initial procedural period with a gain in experience and skill of the interventionist were two significant predictors for success of the procedure in this study.

Acknowledgments

Conflict of interest

The authors report no conflict of interest.

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