

หัตถการการเก็บตัวอย่างเลือดจากหลอดเลือดดำของต่อมหมวกไตในผู้ป่วย ที่มีภาวะอัลโดสเตอโรนสูง : อัตราประสบความสำเร็จทางเทคนิค

ณ โรงพยาบาลมหาราชนครราชสีมา

Adrenal Venous Sampling in Primary Hyperaldosteronism

: Technical Success Rate at Maharat Nakhon Ratchasima Hospital

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บทคัดย่อ

หลักการและเหตุผล : ภาวะที่ต่อมหมวกไตทำงานมากกว่าปกติชนิดที่มีอัลโดสเตอโรนสูง (Primary hyperaldosteronism) มีลักษณะทางคลินิกประกอบด้วย ความดันโลหิตสูง, โพรแตสซีเมียในกระแสเลือดต่ำและมีระดับอัลโดสเตอโรนในพลาสมาสูงขึ้นสัมพันธ์กับระดับเรนินลดลง สาเหตุของภาวะ Primary hyperaldosteronism ที่พบได้บ่อยอาจเกิดจากจากเนื้องอกชนิด Adrenocortical adenoma หัตถการการเก็บเลือดจากเส้นเลือดดำต่อมหมวกไตมีความสำคัญในการช่วยแยกความผิดปกติที่เกิดจากภาวะเนื้องอกชนิด Adrenocortical adenoma ที่หลั่งฮอร์โมนอัลโดสเตอโรนที่เกิดในต่อมหมวกไตข้างใดข้างหนึ่ง จากภาวะต่อมหมวกไตเจริญเติบโตผิดปกติชนิดสองข้าง (bilateral adrenal hyperplasia)

วัตถุประสงค์ : เพื่อประเมินความสำเร็จทางเทคนิคของการทำหัตถการการเก็บเลือดจากเส้นเลือดดำต่อมหมวกไตในผู้ป่วยที่มีภาวะการทำงานของต่อมหมวกไตที่มากกว่าปกติชนิดอัลโดสเตอโรนสูง

วิธีการศึกษา : เป็นการศึกษาวิจัยเชิงพรรณนาและเก็บข้อมูลย้อนหลังในผู้ป่วยที่มีการทำงานของต่อมหมวกไตที่มากกว่าปกติชนิดอัลโดสเตอโรนสูงและได้รับการทำหัตถการการเก็บเลือดจากเส้นเลือดดำต่อมหมวกไตระหว่างเดือนเมษายน พ.ศ. 2556 ถึงเดือนกรกฎาคม พ.ศ. 2561

- ผลการศึกษา** : มีผู้ป่วยจำนวน 18 ราย ในระหว่างเดือนเมษายน พ.ศ. 2556 ถึงเดือน กรกฎาคม พ.ศ. 2561 ซึ่งเป็นเพศชาย 6 ราย เพศหญิง 12 ราย ช่วงอายุระหว่าง 32-67 ปี ที่มีภาวะการทำงานของต่อมหมวกไตที่มากกว่าปกติชนิดที่มีอัลโดสเตอโรนสูงและได้รับการทำหัตถการการเก็บเลือดจากเส้นเลือดดำต่อมหมวกไต หัตถการการเก็บเลือดจากเส้นเลือดดำต่อมหมวกไตประสบความสำเร็จในผู้ป่วย 12 ราย (ร้อยละ 66.7) อัตราประสบความสำเร็จในการเก็บเลือดจากเส้นเลือดต่อมหมวกไตข้างขวาเท่ากับร้อยละ 66.7 และจากเส้นเลือดต่อมหมวกไตข้างซ้ายเท่ากับร้อยละ 100 พบความสำเร็จในการเก็บเลือดจากเส้นเลือดต่อมหมวกไตข้างขวาโดยใช้สายสวนหลอดเลือดสองชนิดในผู้ป่วย 12 ราย พบความสำเร็จในการเก็บเลือดจากเส้นเลือดต่อมหมวกไตข้างขวาโดยใช้วิธีตรวจระดับคอริติซอลขณะทำหัตถการในผู้ป่วย 5 ราย ในผู้ป่วย 6 รายที่ไม่ประสบความสำเร็จในการทำหัตถการการเก็บเลือดจากเส้นเลือดดำต่อมหมวกไตได้รับการผ่าตัดภายหลังจำนวน 2 ราย ไม่พบภาวะแทรกซ้อนจากการทำหัตถการการเก็บเลือดจากเส้นเลือดดำต่อมหมวกไตในผู้ป่วยทุกราย
- สรุป** : หัตถการการเก็บเลือดจากเส้นเลือดดำต่อมหมวกไตในผู้ป่วยที่มีภาวะการทำงานของต่อมหมวกไตที่มากกว่าปกติชนิดที่มีอัลโดสเตอโรนสูงเป็นหัตถการที่มีความปลอดภัยสูงและเพิ่มความสามารถในการประเมินโรคของต่อมหมวกไตว่ามีความผิดปกติที่ต่อมหมวกไตข้างเดียวหรือสองข้าง เทคนิคการทำหัตถการโดยใช้สายสวนหลอดเลือดที่มีความหลากหลายและการวัดระดับคอริติซอลขณะทำหัตถการสามารถช่วยเพิ่มอัตราความสำเร็จในการเก็บเลือดจากเส้นเลือดต่อมหมวกไตข้างขวา
- คำสำคัญ** : ภาวะอัลโดสเตอโรนสูง หัตถการการเก็บเลือดจากเส้นเลือดดำต่อมหมวกไต

วารสารการแพทย์โรงพยาบาลศรีสะเกษ สุรินทร์ บุรีรัมย์ 2563;35(2): 291-302

ABSTRACT

- Background** : Primary hyperaldosteronism is clinical consisted of hypertension, hypokalemia, and increased aldosterone production relative to suppressed plasma renin activity. The causes of primary hyperaldosteronism are most often bilateral adrenal hyperplasia or aldosterone-producing adenoma which require different treatment. Adrenal venous sampling (AVS) is an important tool to differentiate both forms of adrenal disease.
- Objective** : To evaluate the technical success rate of AVS procedure in patients with a clinical presentation of primary hyperaldosteronism
- Methods** : The study was retrospectively reviewed in all patients with clinical of primary hyperaldosteronism and under went AVS, from April 2013-July 2018.
- Results** : From April 2013-July 2018, 18 patients under went AVS (6 men and 12 women, age 32-67 year-old). The success rate of venous sampling in bilateral adrenal veins was 66.7%. The technical success rates of AVS were

66.7% and 100% from the right adrenal vein and the left adrenal vein, respectively. In 5 of 12 patients with success right AVS, two different types of catheter were used. We performed intraprocedural cortisol measurement (IPCM) technique in 7 patients and the right adrenal vein was achieved in 5 patients within the second attempt using the resampling technique. No complication was occurred during and after the AVS procedure.

Conclusion : Adrenal venous sampling is a safe and increasingly utilized procedure in the evaluation of unilateral or bilateral adrenal disease. The success of the procedure can be improved by using a variety of catheters for right adrenal vein cannulation and IPCM with resampling technique.

Keywords : Primary hyperaldosteronism, Adrenal Venous Sampling (AVS)

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Background

Primary hyperaldosteronism is clinical consisted of hypertension, hypokalemia, and increased aldosterone production relative to suppressed plasma renin activity. Patients may present with a variety of clinical abnormality including polyuria, polydipsia, muscle weakness, metabolic alkalosis and uncontrollable hypertension.⁽¹⁾ In clinical practice, primary hyperaldosteronism is one of the cause of secondary hypertension; the prevalence is 2–15% in selected cohorts of hypertensive patients.⁽¹⁻⁵⁾ In the cohort study of the patients with hypertension, the patients who have primary hyperaldosteronism have an increased risk of cardiovascular and cerebrovascular events when compare to the patients with others cause of hypertensive disease.^(5,6) The causes of primary hyperaldosteronism are most often bilateral adrenal hyperplasia or aldosterone producing adenoma, and less common by unilateral adrenal hyperplasia, adrenal carcinoma, or familial hyperaldosteronism.⁽¹⁾

According to the clinical practice guidelines from the Endocrine Society 2016, the patient who is suspected of primary aldosteronism should be underwent screening test, case confirmation and subtype classification.⁽⁷⁾ When the aldosterone-producing adenoma is confirmed from subtype classification, adrenalectomy is a recommended treatment in patients who exhibit lateralization of aldosterone secretion from unilateral aldosterone-producing adenoma, whereas bilateral adrenal hyperplasia requires a mineralocorticoid receptor antagonist.⁽⁷⁾

Adrenal venous sampling (AVS) is the criterion standard to distinguish between unilateral and bilateral adrenal disease in patients with primary aldosteronism.⁽⁷⁾ The AVS procedure is technically challenging and reported success rates to range from 30 to 96%.⁽⁸⁻¹⁰⁾ The success rates of AVS is varying across centers and particularly related to the correct of bilateral adrenal veins cannulation. Blood sampling from the right adrenal vein cannulation is more difficult because of its anatomy and small size.

In Thailand, the reported success rates of AVS on bilateral adrenal venous sampling were 71.9% and 80% in southern and central regions, respectively.^(11,12) The aim of this study is to determine the technical success rate of adrenal venous sampling procedure in patients with a clinical presentation of primary hyperaldosteronism in our Hospital.

Methods

The study was retrospectively reviewed in all patients with clinical of primary hyperaldosteronism and underwent adrenal venous sampling.

Adrenal venous sampling technique

Since April 2013 all adrenal venous sampling procedures were performed by two interventional radiologists (A.T. and C.T.) who had 1 year of experience in interventional radiology. Adrenal venous sampling was performed in the morning. We used continuous adrenocorticotrophic hormone (ACTH) infusion 50 μ /h, initiated 30 minutes before and during the procedure. A 5-French (Fr) vascular sheath was inserted into right femoral vein using the modified Seldinger technique. Blood was sampled from inferior vena cava, left adrenal vein, and right adrenal vein by sequential catheterization. The catheterization of left adrenal vein using a 5-Fr Simmons 2 was done in all cases. A 5-Fr C2 Cobra catheter was usually used for the right adrenal vein. A 5-Fr Shepherd Hook, 5-Fr Headhunter, 5-Fr C1 Cobra, 5-Fr Simmons 1 catheter, or superselective catheterization using microcatheter may be

required. A small amount of contrast material was injected gently into the adrenal veins. After confirmation of the catheter position, intermittent suction from the left adrenal vein and free flow drainage of the blood from the right adrenal veins were performed. The blood was collected about 5 ml from left adrenal vein, 10 ml from inferior vena cava, and at least 2 ml from the right adrenal vein.

We use the strategies as followed for the adrenal venous sampling procedure;

1. Interdisciplinary team includes endocrinologist, radiology Interventionist, urologist, and clinical laboratory technician to review the clinical of the patients and plan of management
2. Review the clinical indication of each patient to perform adrenal venous sampling corresponding to the Endocrine Society Practice Guideline⁽²⁾
3. Review CT anatomy and variation of bilateral adrenal veins
4. The use of Adrenocorticotrophic hormone (ACTH) stimulation 30 minutes before adrenal vein catheterization and throughout the procedure⁽²⁾
5. Using a variety of catheters for right adrenal vein selection
6. Sampling technique : Intermittent gentle suction from left venous blood sampling and free drainage from right venous blood sampling
7. Intraprocedural cortisol measurement (IPCM)⁽³⁾: After the blood was collected from the suspected right adrenal vein, the specimen was immediately sent to the clinical laboratory technician for rapid cortisol measurement.

During the waiting of cortisol level, the vascular sheath on the right femoral vein was not removed. If the selectivity criterion of the right adrenal vein was not achieved, resampling of the right adrenal vein was required on the same day. Due to the waiting time for cortisol level was about 1-2 hours, we use the IPCM technique when the dedicated Angio Suite and clinical laboratory technician were available.

8. Analysis of the Results⁽¹³⁾ : The success rate of AVS was defined as correct catheter position in bilateral adrenal veins which calculated by the formula for selectivity index (SI). The selectivity index was an adrenal vein-to-inferior vena cava cortisol ratio ≥ 5 . Unilateral primary aldosteronism was judged if the gradient of aldosterone-cortisol ratio (Lateralization index) between dominant and non-dominant side was >3.5 .

Table 1 Definition and interpretation of AVS criteria (Adapted from the Endocrine Society guideline2016)⁽¹³⁾

Index	Formula	Interpretation
Selectivity index (SI)	PCC_{side} / PCC_{IVC}	Ratio ≥ 5 confirm that the sample was obtained in the adrenal vein
Lateralization index (LI)	$(PAC_{dominant} / PCC_{dominant})$	Ratio > 3.5 indicate lateralized aldosterone excess

*PCC=plasma cortisol concentration

†PAC=plasma aldosterone concentration

‡IVC= inferior vena cava

Results

From April 2013-July 2018, 18 patients underwent adrenal venous sampling (6 men and 12 women, age 32-67 year-old). The success rate of venous sampling in bilateral adrenal veins was 66.7%. The technical success rates of AVS were 66.7% and 100% from the right side and left side, respectively. The first 14 patients were performed by the first interventionist (A.T.) and the later cases were performed by the second interventionist (C.T). Venous sampling from the right adrenal vein was successful by using a 5-Fr Cobra catheter in 10 patients and a 5-Fr Head Hunter in 2 patients. Venous sampling from the

left adrenal vein was successful in all patients by using a 5-Fr Simmon 2 catheter. We performed intraprocedural cortisol measurement (IPCM) technique in seven patients and the right adrenal vein was achieved in five patients within the second attempt using the resampling technique. Among six patients who failed attempt adrenal venous sampling in bilateral adrenal veins, an adrenal nodule was depicted on CT and underwent surgical adrenalectomy in two patients. No complication was occurred during and after the adrenal venous sampling procedure.

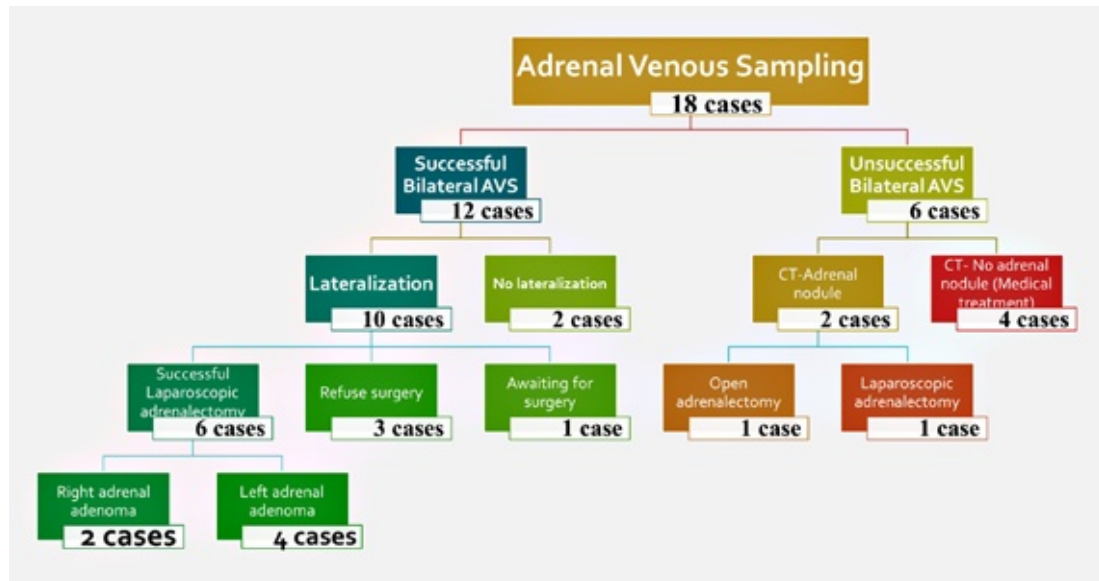


Figure 1 Result of the adrenal venous sampling procedure

Table 2 Characteristics of the patients and result of the adrenal venous sampling procedure

Patient No.	Age (years) / Gender	Successful of AVS	Lateralization	Management	Pathological report
1	50/Male	No	-	Open Adrenalectomy	Left adrenal adenoma
2	43/Female	Yes	No	Medication	-
3	47/Male	No	-	Medication	-
4	59/Male	Yes	Right	Laparoscopic Adrenalectomy	Right adrenal adenoma
5	49/Male	Yes	No	Medication	-
6	54/Female	Yes	Left	Refuse Surgery	-
7	67/Female	Yes	Left	Refuse Surgery	-
8	41/Male	Yes	Left	Refuse Surgery	-
9	57/Female	Yes	Right	Laparoscopic Adrenalectomy	Right adrenal adenoma
10	51/Female	No	-	Medication	-
11	54/Female	No	-	Laparoscopic Adrenalectomy/	Right adrenal adenoma
12	46/Female	Yes	Right	Awaiting surgery	-
13	52/Female	Yes	Left	Laparoscopic Adrenalectomy	Left adrenal adenoma
14	32/Female	Yes	Left	Laparoscopic Adrenalectomy	Left adrenal adenoma
15	67/Female	No	-	Medication	-
16	61/Female	Yes	Left	Laparoscopic Adrenalectomy	Left adrenal adenoma
17	54/Female	Yes	Left	Laparoscopic Adrenalectomy	Left adrenal adenoma
18	56/Male	No	-	Medication	-

Abbreviation: AVS = Adrenal venous sampling

Table 3 The details of AVS procedure including catheter's type, number of sampling position for right adrenal vein, using of IPCM technique and interventionists.

Patient No.	Type of catheter to find right adrenal vein	Type of catheter with successful right adrenal vein catheterization	Number of sampling position for right adrenal vein	IPCM with resampling	Intervention Radiologists
1	5Fr C2 Cobra 5Fr Shepherd Hook	-	3	No	A.T.
2	5Fr C2 Cobra	5Fr C2 Cobra	3	No	A.T.
3	5Fr C2 Cobra	-	3	No	A.T.
4	5Fr C2 Cobra	5Fr C2 Cobra	1	No	A.T.
5	5Fr C2 Cobra 5Fr Headhunter	5Fr C2 Cobra	2	No	A.T.
6	5Fr C2 Cobra 5Fr Headhunter	5Fr C2 Cobra	3	No	A.T.
7	5Fr C1 Cobra 5Fr Shepherd Hook	5Fr C2 Cobra+	3	Yes	A.T.
	5Fr C2 Cobra+ 2.7 Fr Progreat	2.7 Fr Progreat			
8	5Fr C2 Cobra 5Fr C2 Cobra with one side hole 5Fr Headhunter 4Fr C2 Cobra 5Fr Shepherd Hook	5Fr Headhunter	8	Yes	A.T.
9	5Fr C2 Cobra 5Fr Headhunter	5Fr C2 Cobra	2	Yes	A.T.
10	5Fr C2 Cobra with sidehole 5Fr Headhunter	-	5	Yes	A.T.
11	5Fr C2 Cobra 5Fr Headhunter	-	1	Yes	A.T.
12	5Fr C2 Cobra 5Fr Headhunter	5Fr C2 Cobra	2	Yes	A.T.
13	5Fr C2 Cobra 5Fr Headhunter	5Fr Headhunter	3	Yes	A.T.
14	5Fr C2 Cobra	5Fr C2 Cobra	2	No	A.T.
15	5Fr C2 Cobra 5Fr Shepherd Hook+ 1.98 Fr Parkway	-	3	No	C.T.
16	5Fr C2 Cobra	5Fr C2 Cobra	6	No	C.T.
17	5Fr C2 Cobra	5Fr C2 Cobra	6	No	C.T.
18	5Fr C2 Cobra 5Fr Shepherd Hook	-	6	No	C.T.

Abbreviation: AVS = Adrenal venous sampling, Fr = French, IPCM = intraprocedural cortisol measurement

Table 4 A 59 year-old man (Patient No.4) with primary hyperaldosteronism and a right adrenal nodule on CT study was performed adrenal venous sampling. The adrenal venous sampling revealed right lateralization.

Vein	Aldosterone, mo/L	Cortisol, mo/L	Selectivity index	Adrenal vein PAC-to- PCC ratio	Lateralization index
Right adrenal vein	3,146	153	153/25= 6.12	3,146/153= 20.5 (dominant)	41
Left adrenal vein	175	337	337/25=13.48	337/175= 0.5 (non-dominant)	-
Inferior vena cava	-	25	-	-	-

Abbreviation: PCC=plasma cortisol concentration, PAC=plasma aldosterone concentration, IVC= inferior vena cava

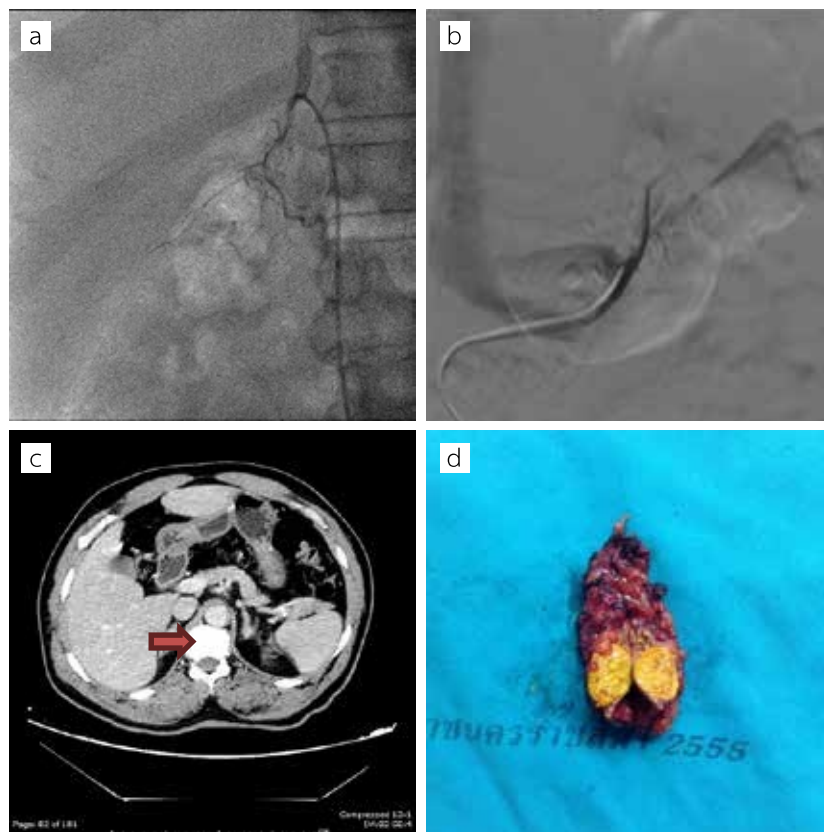


Figure 2 A 59 year-old man with primary hyperaldosteronism and a right adrenal nodule on CT study was performed adrenal venous sampling. The adrenal venous sampling showed right lateralization. Laparoscopic right adrenalectomy was successfully performed. (a) Angiogram of right adrenal vein. (b) Angiogram of left adrenal vein. (c) CT study showed right adrenal nodule (arrow). (d) Gross specimen of right adrenal gland showed yellowish nodule which was consistent with adrenal adenoma.

Discussion

The success rate of venous sampling in bilateral adrenal veins was 66.7% in our study which was lower than the reported of 71.9% by Chayovan T et al.⁽¹¹⁾ and 80% by Kongphanich et al.⁽¹²⁾ Unsuccessful AVS was primarily due to failure in cannulating the right adrenal vein. There were several factors related to adrenal venous sampling procedure in our centre which affect the outcome. Low volume of patients and low experience of the interventionists could be the factors that decreased the success rate. AVS has performed about 3-4 cases per year in our centre, whereas Chayovan T. et al.⁽¹¹⁾ reported 7-9 procedures per year and Stowasser M. et al.⁽¹⁴⁾ suggested that the focused technical expertise should maintain skill at least 15-20 procedures per year. The number and experience of the interventionist were also the keys to AVS success. The report by Chayovan T et al.⁽¹¹⁾ showed the higher success rate of bilateral AVS in a dedicated single interventionist and previous studies suggested that the AVS procedure should be limited to a few interventionists particularly in a low-volume centre^(8,11). The study in the learning curve of a single interventionist by Jakobsson et al.⁽¹⁵⁾ reported the satisfactory AVS success rate was achieved after 36 procedures and increased success rate to more than 96% after 7 years with 18-36 AVS procedures per year.

The studies by Chayovan et al.⁽¹¹⁾ and Berney et al.⁽¹⁶⁾ reported that the male gender was the factor associated with the success of AVS about ten times more likely to succeed than in females. In our study, the success rate in the female gender was higher than in male patients. However, the result in our study may be limited

by a small number of patients.

The study by Omura et al.⁽¹⁷⁾ revealed the variation of right adrenal vein anatomy in its location and angle. The orifice of the right adrenal vein was located between the T10 and L1 vertebrae, 99% in the right posterior quadrant, and most common frequent angle in a posterior, rightward, and caudal course.⁽¹⁷⁾ Different types of catheter may increase the success rate in the right adrenal vein cannulation. The right adrenal vein was successfully cannulated using a 5-Fr C2 Cobra catheter in most of our cases. However, two cases were success after changing the catheter to 5-Fr Head Hunter type. Regarding to the studies using a three-dimensional (3D) type catheter, the results were promising which the 3D shape improved the stability of the catheter in the IVC.^(18,19) Araki et al.⁽¹⁹⁾ studied the use of two type catheters (planar and 3D shape) and showed an 83% success rate in right adrenal vein cannulation using one or both type catheters.

Increased rate of success AVS using Intraprocedural cortisol measurement (IPCM) was reported in previous publications.^(20,21) We performed the IPCM technique in seven patients and the right adrenal vein was achieved in five patients within the second attempt using the resampling technique. To use the IPCM technique need the available and collaboration of interventional radiology team, laboratory transportation and the clinical laboratory clinician. The procedure time may be prolonged when use IPCM technique.

Adjunctively use of C-arm CT was another technique to increase the success rate of bilateral adrenal venous sampling which

reported elsewhere.^(22,23) However, the C-arm CT was not available in our center.

The complications such as rupture of the adrenal vein, adrenal infarction, adrenal vein thrombosis, hypertensive crisis, and adrenal insufficiency could occurred in AVS procedure. However, complications of AVS procedure are rare, occurring less than 1%.^(24,25) No complication was found in our study.

There were some limitations in this study. First is a low volume of patients who underwent AVS procedure in our centre which may reflect that the AVS is underused. Second, the findings of adrenal nodules on CT images did not be evaluated or compared with AVS or surgical results. Third, the outcome of the patients in blood pressure control after adrenalectomy was not reviewed. However, improved blood pressure control in nearly all patients who undergo AVS-guided adrenalectomy was reported in previous studies.^(26,27)

Conclusion

Adrenal venous sampling is a safe and increasingly utilized procedure in the evaluation of unilateral or bilateral adrenal disease. The success of the procedure can be improved by using a variety of catheters for right adrenal vein cannulation and Intraprocedural cortisol measurement (IPCM) with resampling technique.

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