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## Clinical Management and Outcomes of Adrenal Hemorrhage Following Adrenal Vein Sampling in Primary Aldosteronism

### This is the author's manuscript

*Original Citation:*

*Availability:*

This version is available <http://hdl.handle.net/2318/1590661> since 2016-09-01T12:54:04Z

*Published version:*

DOI:10.1161/HYPERTENSIONAHA.115.06305

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(Article begins on next page)

1 **Clinical management and outcomes of adrenal haemorrhage following adrenal vein sampling**  
2 **in primary aldosteronism.**

3 Silvia Monticone\*, Fumitoshi Satoh\*, Anna S. Dietz, Remi Goupil, Katharina Lang, Francesca  
4 Pizzolo, Richard D. Gordon, Ryo Morimoto, Martin Reincke, Michael Stowasser\*\*, Paolo  
5 Mulatero\*\*.

6 \* and \*\* equal contribution

7 **Affiliations**

8 Division of Internal Medicine and Hypertension (S.M., P.M.), Department of Medical Sciences,  
9 University of Torino, Torino, Italy; Division of Clinical Hypertension, Endocrinology & Metabolism  
10 (F.S., R.M.), Tohoku University Graduate School of Medicine, Sendai, Japan; Endocrine  
11 Hypertension Research Centre (R.G., R.D.G., M.S.), University of Queensland School of Medicine,  
12 Greenslopes and Princess Alexandra Hospitals, Brisbane; Unit of Internal Medicine (F.P.),  
13 Department of Medicine, University of Verona, Verona, Italy; Department of Internal Medicine I  
14 (K.L.), University Hospital Wuerzburg, Wuerzburg, Germany; Medizinische Klinik und Poliklinik  
15 IV (A.S.D., M.R.), Ludwig-Maximilians-Universität, Munich, Germany.

16 **Short title:** Adrenal haemorrhage in primary aldosteronism

17 **Abbreviations:** PA: primary aldosteronism; EH: essential hypertension; AVS: adrenal vein  
18 sampling; APA: aldosterone producing adenoma; BAH: bilateral adrenal hyperplasia; AH: adrenal  
19 hemorrhage.

20 **Word count:** abstract 246 words, manuscript: 5799 words

21 **Number of figures/tables:** 1 figure, 2 tables

22 **Corresponding author and person to whom reprints should be addressed:**

1 Paolo Mulatero, Division of Internal Medicine and Hypertension, Department of Medical Sciences,  
2 University of Torino.  
3 Via Genova 3, 10126, Torino, Italy  
4 Phone: +39-0116336959 Fax: +39-0116336031  
5 [paolo.mulatero@libero.it](mailto:paolo.mulatero@libero.it)

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1 **Abstract**

2 Aldosterone-producing adenoma and bilateral adrenal hyperplasia account for more than 90% of all  
3 primary aldosteronism cases. Distinguishing between bilateral and unilateral disease is of  
4 fundamental importance because it allows targeted therapy. Adrenal vein sampling is the only reliable  
5 means to preoperatively differentiate between unilateral and bilateral subtypes. A very rare but  
6 serious complication of adrenal vein sampling is an adrenal haemorrhage. We retrospectively  
7 examined in detail 24 cases of adrenal haemorrhage during adrenal vein sampling in 6 different  
8 referral hypertension centers. Adrenal haemorrhage more often affected the right adrenal (n=18) than  
9 the left (n=5, P<0.001; 1 bilateral). Median duration of experience of the radiologist in adrenal vein  
10 sampling at the time of adrenal haemorrhage was 5.0 years [0.6-7.8] and adrenal haemorrhage  
11 occurred with both highly experienced (>10 yrs) and less experienced radiologists. Of 9 patients who  
12 suffered adrenal haemorrhage in the gland contralateral to an aldosterone-producing adenoma and  
13 who underwent complete (n=6) or partial (n=3) unilateral adrenalectomy, only one required long-  
14 term corticosteroid replacement for adrenal insufficiency. No reduction in blood pressure or  
15 biochemical resolution of primary aldosteronism occurred in any of those patients who experienced  
16 adrenal haemorrhage in the gland ipsilateral to an aldosterone-producing adenoma (n=6) or who had  
17 bilateral adrenal hyperplasia (n=9). No patient required invasive treatments to control bleeding or  
18 blood transfusion. In conclusion, adrenal haemorrhage usually has a positive outcome causing either  
19 no or minor effects on adrenal function and adrenal vein sampling should remain the best approach  
20 to primary aldosteronism subtype differentiation.

21

22 **Key words:** primary aldosteronism, adrenal vein sampling, aldosterone-producing adenoma, bilateral  
23 adrenal hyperplasia, adrenal hemorrhage

24

25

## 1 **Introduction**

2 Studies both *in vivo* and *in vitro* have demonstrated that aldosterone plays a detrimental role on the  
3 cardiovascular system and patients affected by primary aldosteronism (PA) have an increased rate of  
4 cardio- and cerebro-vascular complications compared to essential hypertensives with a similar blood  
5 pressure levels (1, 2). In light of these considerations, the early identification of PA is crucial to enable  
6 targeted treatment to reverse the excess of organ damage in affected patients. As detailed by the  
7 Endocrine Society (3) and by the Japanese Endocrine Society Guidelines (4), optimal management  
8 of PA patients is dependent on the differentiation between aldosterone-producing adenoma (APA)  
9 and bilateral adrenal hyperplasia (BAH), the two most common subtypes of sporadic PA.

10 Adrenal CT scanning with contrast and fine cuts is recommended in all confirmed PA patients to rule  
11 out malignancy (aldosterone-producing adrenocortical carcinoma), but it is otherwise unreliable for  
12 subtype differentiation since it lacks both sensitivity and specificity. In particular, micro-adenomas  
13 (< 1 cm in diameter) can be overlooked and it is not possible to distinguish between non-secreting  
14 incidentalomas and APAs by adrenal CT scanning alone (3,5).

15 Adrenal vein sampling (AVS) is a demanding procedure consisting of the selective cannulation of the  
16 adrenal veins to identify the source of aldosterone overproduction. It was first described in the 1960s  
17 as a technique to localize APAs preoperatively (6), but its inherent invasiveness, lack of standardized  
18 criteria for interpretation of the hormonal results and the reported high complication rates at that time  
19 were major factors in hindering its employment in the clinical management of PA. A complication of  
20 AVS is adrenal haemorrhage (AH), secondary to adrenal vein rupture or, less frequently, to  
21 dissection, infarction or thrombosis (7).

22 Historically, complication rates ranged between 5% to 10% and were reportedly associated with  
23 complete and permanent destruction of the gland (8-10). More recent studies, however, report a  
24 substantially lower rate of complications of between 0.2 to 0.9% (7,11). In part, this is likely to be  
25 related to the advent of CT for the imaging of adrenal lesions and the consequent abandonment of the  
26 practice of retrograde adrenal venography which required injection of a relatively large amount of

1 contrast under considerable pressure, and was associated with an increased risk of AH (7).  
2 Interestingly, a recent observational, retrospective, multicenter study demonstrated that the rate of  
3 adrenal vein rupture was not predicted by the method of cannulation, but rather by the experience of  
4 the radiologist, that is, the number of AVS performed by each radiologist (7).  
5 Despite an impressive number of studies comparing the performances of imaging techniques and  
6 AVS in the subtype differentiation of PA (12), a systematic study on AH has never been performed  
7 and uncertainties in the clinical management of this complication still remain. The aim of this study  
8 was to describe the clinical presentation, management and outcome of 24 AH cases, collected from 6  
9 different tertiary referral hypertension centers, to help clinicians decide whether to use AVS in their  
10 PA patients.

11

## 12 **Materials and methods.**

### 13 **Patients selection.**

14 We retrospectively evaluated 24 cases of adrenal haemorrhage following AVS that occurred in 6  
15 tertiary referral hypertension centers in Italy (Torino, 1994-01/2015, 427 AVS; Verona, 2009-2014,  
16 31 AVS), Germany (Munich, 12/2009-01/2015, 255 AVS; Wuerzburg 12/2009-01/2015, 69 AVS),  
17 Japan (Sendai, 04/2007-12/2014, 640 AVS) and Australia (Brisbane, 1990-2014, 1446 AVS).

18 The control group comprised 1388 PA patients who underwent AVS in the different centres  
19 participating in the study, during a similar period of time as when the patients experienced AH during  
20 AVS (supplemental Table S1).

21 The diagnosis of PA was made according to the Endocrine Society and the Japanese Endocrine  
22 Society Guidelines (3,4). Confirmatory testing and synacthen test were performed as detailed  
23 elsewhere (13-15).

1 All patients included in the analysis gave written informed consent and approval from the local ethics  
2 committees was obtained for the use of these retrospective data. The study adhere to the principles of  
3 the Declaration of Helsinki and and to institutional guidelines.

4 An expanded methods section is given in the supplemental file.

5

## 6 **Statistical analyses**

7 IBM SPSS Statistics 19 (SPSS INC, Chicago, IL) was used for statistical analyses. Data are presented  
8 as mean  $\pm$  standard error or median (25th-75th percentile). Data were analyzed with the Kolmogorov-  
9 Smirnov and Shapiro-Wilk tests to determine their distributions. Statistical significance between  
10 groups was calculated in normally distributed data by a Student *t* test for independent samples and in  
11 not normally distributed data by the Kruskal-Wallis test, using Bonferroni corrections for multiple  
12 comparisons. The chi-square test of the Fisher exact test were used for qualitative variables. A  
13 probability value of less than 0.05 was considered statistically significant.

14

## 15 **Results.**

### 16 **General description of the cases.**

17 We retrospectively identified 24 cases of adrenal haemorrhage that occurred during AVS in 6  
18 different referral hypertension centers in Italy, Germany, Japan and Australia. Clinical and  
19 biochemical characteristics (before and after AVS) of the patients included in the study are  
20 summarized in Tables 1 and 2.

21 In our series, AH was more frequent in the right adrenal (n=18) than in the left (n=5, P<0.001), and  
22 in one case AH was bilateral. In one case (MU-01) the patient was referred for super-selective adrenal  
23 vein sampling because of bilateral nodules at adrenal computed tomography (CT) scanning but lack  
24 of lateralization at previous, non-selective AVS. Haemorrhage occurred during the catheterization of  
25 side branches of the right adrenal vein. AVS showed highest aldosterone/cortisol-ratios in a vein  
26 draining the lateral limb of the right adrenal which bore an adenoma. In another case of right AH

1 (BR-1), for the AVS procedure, gadolinium was used instead of iodinated contrast due to concerns  
2 about contrast allergy.

3 CT scanning of a patient (TO-01) with right AH and left APA is shown in figure 1.

4 Patients experiencing AH were older than patients who underwent uncomplicated AVS procedures.  
5 None of the other assessed clinical or biochemical and hormonal parameters were significantly  
6 different between the AH and the controls (supplemental table 1). Of the 24 patients included in the  
7 study, two were taking aspirin 100 mg/day (WU-01 and MU-03) one of whom was also under  
8 treatment with enoxaparin 0.4 mg (MU-03) (of note the percentage of patients on aspirin was not  
9 significantly different from the percentage of total PA patients receiving aspirin treatment within the  
10 Torino unit; data not shown); no other patients were receiving medications that are likely to have  
11 affected coagulation or platelet aggregation thereby facilitating the occurrence of AH. In our series  
12 there were no significant comorbidities other than diabetes in one patient (BR-10) and polymyalgia  
13 rheumatica treated with steroids in another (MU-03).

14 According to AVS results, the final diagnosis was bilateral adrenal hyperplasia in 9 patients, left APA  
15 in 8 patients and right APA in 7 patients. In two patients (BR-7 and SE-03) the first AVS was not  
16 diagnostic: in BR-7 the right adrenal vein was not cannulated and in SE-03 the AVS was stopped  
17 after the occurrence of adrenal vein rupture. Repeated AVS revealed a final diagnosis of BAH in SE-  
18 03 and left APA in BR-7.

19 The median duration of experience of the radiologist in AVS at the occurrence of the AH was 5.0  
20 years [0.6-7.8, 25<sup>th</sup>-75<sup>th</sup> percentile] and, at the time of AH, 33% (8/24) of the radiologists performed  
21 less than 10 AVS/year, while 67% (16/24) performed more than 10 AVS/year.

22 In all but 2 patients, the occurrence of AH required hospitalization or a prolongation of hospital stay  
23 compared to non-complicated procedures for an average of 1.9±1.3 days. Overall 54% (13/24) of the  
24 patients required the administration of a strong opioid (morphine, pethidine, piritramide, fentanyl) for  
25 efficient pain management, 8% required the administration of a weak opioid (codeine, tramadol),  
26 while 38% (9/24) required no analgesic medications. After the diagnosis of AH, adrenal CT was



1 performed in 16 patients, one of whom also underwent NP-59 adrenal scintigraphy, to evaluate the  
2 residual activity of the affected adrenal gland. In 8 patients imaging was not performed. In our series  
3 none of the patients required invasive treatments to control bleeding or blood transfusion because of  
4 anaemia.

5 **Final diagnosis of unilateral PA, AH contralateral to the adenoma.**

6 Of the 15 patients displaying unilateral disease, AH occurred in the contralateral side to the adenoma  
7 in 9 cases. None of the 9 patients with AH contralateral to the side of lateralization showed BP  
8 reduction after the occurrence of the AH. Three of these 9 patients underwent nodulectomy and 6  
9 underwent total laparoscopic adrenalectomy. In all patients who underwent total adrenalectomy and  
10 had AH contralateral to the adenoma, adrenal function was tested to rule out adrenal insufficiency.  
11 Plasma cortisol at 8:00 a.m. was within the normal range (5-25 mg/dL) in all patients; rapid synacthen  
12 test was normal in five of the six tested patients (normal values > 500 nmol/L, 18.1 mcg/dL). In two  
13 patients (with right AH, BR-01 and BR-10) left adrenalectomy was performed under hydrocortisone  
14 cover. In the immediate post-operative period, patient BR-10 received ongoing treatment with  
15 dexamethasone while undergoing a short synacthen test (which showed a very blunted response from  
16 <35 to 83 nmol/L) followed by a “long synacthen test” (0900h cortisol levels basally and daily for  
17 two days after commencement of intramuscular depot tetracosactrin, 1 mg 12 hourly). Because the  
18 latter demonstrated a definite (albeit modest) cortisol response (from <35 to 306 nmol/L by day 1 and  
19 271 nmol/L by day 2), dexamethasone was gradually withdrawn but an adrenal crisis occurred  
20 following subsequent shoulder surgery and the patient was therefore commenced (and remains) on  
21 cortisol and fludrocortisone supplementation. In patient BR-01 the test was performed 5 days after  
22 adrenalectomy and demonstrated a sub-normal response (from 303 to 484 nmol/L) and he therefore  
23 remained on glucocorticoid supplementation with plans for repeat testing in six weeks’ time. Adrenal  
24 function was also assessed in all patients who underwent nodulectomy (n=3) (in one case, WU-01 the  
25 tests were performed and reported as normal, but hormonal values were not available) and was found  
26 to be normal in each case (in BR-11 short synacthen test 1 month after adrenalectomy showed a

1 partially blunted response after 60 minutes; the test was repeated 4 months later and showed an  
2 adequate response). In one patient (TO-01) NP-59 adrenal scintigraphy performed without  
3 dexamethasone suppression demonstrated a focus of tracer uptake by the right adrenal in agreement  
4 with residual right adrenal cortex function (Supplemental Figure S3): this patient had a normal  
5 synacthen test after nodulectomy. Of the three patients who underwent nodulectomy, two became  
6 normotensive without any anti-hypertensive medication and one displayed significant improvement  
7 of hypertension (normotensive on irbesartan 150 mg/day, before adrenalectomy SBP 180 mmHg,  
8 DBP 100 mmHg on three anti-hypertensive medications). Of the 6 patients who underwent total  
9 unilateral adrenalectomy, one displayed long-term adrenal insufficiency (BR-10) but BR-01, who  
10 demonstrated a blunted cortisol response to synacthen in the early post-operative period requires  
11 repeat testing to assess whether normal adrenal function has returned (adrenalectomy performed in  
12 March 2015). Four patients were cured of PA and hypertension, 1 displayed significant amelioration  
13 of blood pressure levels and biochemical cure of PA and 1 was operated only in March 2015 and has  
14 not been fully re-evaluated after the operation.

15 **Final diagnosis of unilateral PA, AH ipsilateral to the adenoma.**

16 Of the 15 patients displaying unilateral disease, AH occurred in the side of the adenoma in 6 cases.  
17 According to the historical reports indicating permanent adrenal dysfunction after AH, we would  
18 have expected that AH in the side of the adenoma to have resulted in cure of PA without further  
19 treatment. However in our series, none of the patients displayed cure of PA or improvement of  
20 hypertension following AH, and all patients therefore still required unilateral adrenalectomy.  
21 Consistently, aldosterone levels did not change significantly after the AH but before the  
22 adrenalectomy in the four out of six patients who had the hormone tested (Supplemental Table S2).  
23 The occurrence of the AH was confirmed in all cases by histology report, clearly showing presence  
24 of recent bleeding in both the tumor and the adjacent adrenal tissue. None of these patients had  
25 evidence of adrenal insufficiency, as expected.

26 **Final diagnosis of BAH.**

1 In a recent report, hypertension was improved in 14 of 40 patients with BAH who underwent  
2 unilateral adrenalectomy (16). We analyzed the post-AVS parameters of the 9 BAH patients who  
3 experienced unilateral AH. Of note, none of the patients displayed any degree of blood pressure  
4 reduction or amelioration of PA after unilateral AH. As expected, we did not detect signs or symptoms  
5 of adrenal insufficiency in these patients.

6

## 7 **Discussion.**

8 The diagnosis of PA is a three step process (screening, confirmation and subtype differentiation) and  
9 AVS is recognized by the Endocrine Society and Japanese Endocrine Society Guidelines (3,4) as the  
10 gold standard test to distinguish between unilateral and bilateral disease. It is a demanding  
11 interventional procedure where the adrenal veins are accessed through a femoral vein approach and  
12 cannulated to identify the source of aldosterone overproduction. The left adrenal vein almost always  
13 drains into the left renal vein and it is therefore usually relatively easy to cannulate. On the contrary,  
14 the right adrenal vein is small, drains directly into the inferior vena cava and it is therefore more  
15 difficult to cannulate (17). Moreover, despite significant efforts towards standardization, AVS  
16 protocols and interpretation of hormone results vary widely across centers (5,12).

17 Adrenal vein rupture and subsequent AH represent the most serious complication of AVS. Despite  
18 being now widely recognized that the prevalence of AH is not as high as suggested by historical  
19 reports, the clinical outcomes of this complication have never been systematically investigated and  
20 evidence on the subsequent optimal management is still lacking.

21 In this study we collected 24 cases of AH through 6 different referral hypertension centers in Italy,  
22 Germany, Japan and Australia and retrospectively investigated the clinical management and the  
23 outcomes in terms of hospital stay, need for medications/interventional procedure and the rate of  
24 complete and permanent destruction of the affected adrenals. Interestingly, as suggested by historical  
25 reports (9) we observed that AH occurred more frequently in the right adrenal vein suggesting that  
26 the anatomy, unfavorable for cannulation, can at least partially account for this difference. In addition,

1 the higher number of attempts necessary to cannulate the right adrenal vein may have contributed to  
2 the higher rate of AH. Overall, abdominal pain was the most common symptom associated with the  
3 occurrence of AH and required treatment with strong opioids in the majority of the patients. Follow  
4 up imaging was performed in most patients, mainly by CT scanning. Only in one case was functional  
5 evaluation by adrenal scintiscan performed. In this patient the uptake of the tracer in the adrenal  
6 containing the AH demonstrated that the complication did not result in loss of functional activity of  
7 the gland.

8 A recent observational retrospective multicenter study (7) showed that the rate of adrenal vein rupture  
9 was inversely correlated with the number of procedures performed by each radiologist and directly  
10 with the number of AVS procedures performed per center. However, in our series AH occurred with  
11 both experienced radiologists (> 5 years of experience and > 10 procedures/year) and inexperienced  
12 ones, consistent with experience of the operator being not the only important factor associated with  
13 the occurrence of AH.

14 It should be noted that in two patients with AH, AVS was successfully and uneventfully repeated  
15 without complication, showing that a previous AH does not necessary exclude the feasibility of a  
16 subsequent AVS.

17 The most important finding of this study is represented by the outcome data regarding the residual  
18 function of the affected adrenal. In our series of 24 AH only one patient, after removal of the adrenal  
19 contralateral to the AH, displayed signs and symptoms of adrenal insufficiency, requiring long-term  
20 therapy with replacement doses of hydrocortisone. In another case operated in March 2015 the  
21 synacthen test was slightly suboptimal and the patient will be subsequently re-evaluated by repeat  
22 testing. These findings show that the functional activity of the adrenals after the haemorrhage is in  
23 most cases not markedly impaired by this complication. In agreement with these findings we did not  
24 observe a blood pressure reduction after the AH when the event involved the adrenal bearing the APA  
25 or in BAH patients.

1 In clinical practice, when the AH involves the contralateral adrenal to an APA the clinician may be  
2 concerned about the residual adrenal function of the affected adrenal gland and hence whether  
3 cortico steroid replacement will be required peri-operatively and long-term following unilateral  
4 adrenalectomy. One option is to perform an adrenal-sparing nodulectomy to save part of the  
5 functioning cortex surrounding the APA. However, this surgical option has the potential disadvantage  
6 of PA persisting if the removed nodule was not the sole source of excessive aldosterone production  
7 (18). In fact, aldosterone production outside the main nodule of the removed adrenal was observed in  
8 immunohistochemistry studies using specific antibodies for CYP11B2 (19,20). To overcome this  
9 disadvantage, super selective segmental adrenal vein branches AVS would be required (21).  
10 However, this technique is highly demanding and is only available in few specialized centres (22). In  
11 addition to performing short synacthen testing post-operatively, pre-operative testing for residual  
12 adrenal function in the gland bearing the AH by performing adrenal scintiscan using <sup>131</sup>I-nor  
13 cholesterol (NP59) without dexamethasone suppression could be considered. This procedure has been  
14 suggested previously (23) and successfully undertaken in one of our patients (TO-01) before  
15 contralateral adrenalectomy to the AH. Furthermore, the identification of the anatomy of right adrenal  
16 vein by contrast-enhanced multidetector CT before AVS may be helpful to shorten the time required  
17 for AVS performance, thereby reducing the AH risk (11,24). Finally, in some selected cases in which  
18 the clinical, radiological and biochemical information point strongly towards unilateral APA, a case  
19 for avoiding AVS could be made (11,24-28).

20 The main limitation of the present study is the retrospective nature of data collection; therefore the  
21 evaluation of patients' outcome after the adrenal haemorrhage was not standardized.

22

23 In conclusion, to the best of our knowledge this represents the first study undertaken primarily to  
24 explore the management and the outcomes of AH occurring during AVS. AH, despite being the most  
25 dreaded complication of AVS, usually has a positive outcome causing minor or no permanent effects

1 on adrenal function and should not discourage clinicians from using AVS to correctly diagnose the  
2 PA subtype.

3

#### 4 **Perspectives**

5 A wealth of studies clearly demonstrated that PA is the most frequent cause of secondary  
6 hypertension. AVS is the only reliable way of differentiating unilateral PA forms that benefit from  
7 adrenalectomy from bilateral forms that are treated pharmacologically. AVS is currently performed  
8 in few referral centres: one of the obstacles to the wide acceptance of this technique is the invasive  
9 nature of the procedure that in some cases is complicated by AH. In the present study this rare  
10 complication usually had a positive outcome in terms of adrenal function. Therefore, AVS should be  
11 offered to all PA patients that are considered for unilateral adrenalectomy,

12

13 **Source of Funding:** This study was funded by a grant from MIUR 2013 (ex 60%, Ministry of  
14 Instruction, University and Research, Italy, to P.M.) and by a grant from MIUR 2014 (ex-60%,  
15 Ministry of Instruction, University and Research, Italy, to S.M.). The German Conn Registry-Else  
16 Kröner-Fresenius-Hyperaldosteronismus Registry is supported by a grant from Else Kröner-  
17 Fresenius-Stiftung to MR (2013\_A182). R.G. received salary support from the Fonds de recherche  
18 du Québec en santé and the Société québécoise d'hypertension artérielle.

19 **Disclosure summary:** the authors have nothing to disclose

20

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## 6 **Novelty and Significance:**

### 7 **What Is New**

- 8 • Adrenal haemorrhage (AH) following AVS in primary aldosteronism is a rare event and is  
9 more frequent in the right adrenal than in the left and in older patients.
- 10 • None of the patients affected by AH on the side of the adenoma displayed cure of PA or  
11 improvement of hypertension following AH.
- 12 • The occurrence of AH required hospitalization or a prolongation of hospitalization  
13 compared to non-complicated procedures and required treatment with strong opioid for  
14 efficient pain management in the majority of patients.
- 15 • Only one patient, after removal of the adrenal contralateral to the AH, displayed signs and  
16 symptoms of adrenal insufficiency, requiring long-term therapy with replacement doses of  
17 hydrocortisone.

### 20 **What Is Relevant**

- 21 • AH usually has a positive outcome causing either none or only minor permanent effects on  
22 adrenal function. Therefore, AVS should remain the favoured approach to PA subtype  
23 differentiation.

1 **Summary**

2 Adrenal haemorrhage is a rare complication of adrenal vein sampling for subtype diagnosis of  
3 primary aldosteronism and usually is followed by a favourable outcome in term of adrenal function.

4

5 **Legend to figures.**

6 **Figure 1.** CT scan just after AVS in patient TO-01.

7 Panel A: left adrenal gland with a discrete 1 cm-diameter nodule at the lateral gland limb (arrow).

8 Panel B: right supra-renal space is almost completely filled by an oval hematoma (arrow-head).

9 Two different cuts are shown because adrenal glands were situated in on different CT planes.

10

11

<b>Patients</b>	<b>Age at AVS (years)</b>	<b>Sex</b>	<b>SBP/DBP (number of drugs) before AVS</b>	<b>Experience of the radiologist in AVS at the time of the AH (years)</b>	<b>Year of the AH</b>	<b>Side of AH</b>	<b>Diagnosis at AVS</b>
BR-01	41	M	143/88 (3)	8	2013	Right	Left APA
BR-02	41	M	180/110 (4)	3	1992	Right	BAH
BR-03	45	M	155/105 (3)	< 1	1992	Right	Right APA
BR-04	69	M	154/84 (1)	< 1	1994	Right	BAH
BR-05	65	M	136/80 (4)	< 1	1992	Right	BAH
BR-06	58	F	110/80 (2)	< 1	1995	Bilateral	BAH
BR-07	53	M	154/98 (3)	1	1995	Left	N.D.*
BR-08	60	F	162/84 (3)	2	1997	Left	Left APA
BR-09	58	F	141/64 (2)	5	1999	Right	BAH
BR-10	67	M	180/94 (3)	6	2000	Right	Left APA
BR-11	68	M	140/90 (1)	18	2013	Right	Left APA
BR-12	51	M	155/80 (0)	15	2010	Left	Right APA
MU-01	35	F	130/85 (1)	5	2014	Right	Right APA
MU-02	62	F	184/83 (1)	<1	2014	Right	Right APA
MU-03	76	M	170/80 (3)	<1	2014	Right	BAH
MU-04	55	M	160/103 (2)	5	2012	Right	Right APA
WU-01	52	M	180/100 (3)	7	2000	Right	Left APA
SE-01	63	F	155/87 (1)	8	2008	Right	Left APA
SE-02	66	M	161/86 (2)	10	2010	Left	Right APA
SE-03	55	F	126/79 (4)	7	2009	Right	N.D.§
SE-04	62	M	140/83 (2)	7	2007	Left	Right APA
SE-05	71	M	158/90 (1)	4	2008	Right	BAH
TO-01	55	M	180/120 (2)	15	2012	Right	Left APA
VE-01	49	M	130/90 (2)	2	2014	Right	BAH
All	57±11	-	153/89 (2)	5.0 [0.6-7.8]			

**Table 1. Clinical parameters of patients with adrenal haemorrhage**

\* The AVS was repeated and then lateralized to the left; § The AVS was repeated and showed bilateral disease

SBP = systolic blood pressure; DBP = diastolic blood pressure; AH = adrenal haemorrhage; CT = computed tomography; N.D. = not diagnostic; AVS = adrenal vein sampling .

<b>Patients</b>	<b>Hospitalization requirement (days)</b>	<b>Drugs for pain control</b>	<b>Follow up imaging</b>	<b>Adrenalectomy</b>	<b>Same side/CL side</b>	<b>SBP/DBP (no. classes of drugs) after AVS/ADX</b>
BR-01	Yes (1)	Morphine s/c, paracetamol	CT scan	Yes	CL side	182/116 (3)
BR-02	Yes (2)	Pethidine, paracetamol	CT scan	No	N.A.	160/80 (4)
BR-03	Yes (3)	Pethidine, omnopon	CT scan	Yes	Same side	156/110 (1)
BR-04	Yes (1)	Pethidine	CT scan	No	N.A.	160/80 (1)
BR-05	Yes (2)	Morphine s/c, paracetamol	CT scan	No	N.A.	192/96 (5)
BR-06	No	Pethidine, paracetamol	None	No	N.A.	130/68 (2)
BR-07	No	None	None*	Yes	Same side	164/88 (2)
BR-08	Yes (1)	Pethidine, paracetamol	CT scan	Yes	Same side	124/84 (0)
BR-09	Yes (1)	Pethidine, paracetamol	CT scan	No	N.A.	157/94 (3)
BR-10	Yes (5)	Codeine, paracetamol	CT scan	Yes	CL side	134/78 (0)
BR-11	Yes (2)	Paracetamol, pethidine	CT scan	No (nodulectomy)	CL side	140/80 (0)
BR-12	Yes (3)	Paracetamol, pethidine	CT scan	Yes	CL side	128/85 (0)
MU-01	Yes (1)	Metamizol	None	No (nodulectomy)	Same side	113/76 (0)
MU-02	Yes (1)	None	None	Yes	Same side	130/85 (0)
MU-03	Yes (3)	Paracetamol	CT scan	No	N.A.	145/65 (3)
MU-04	Yes (3)	Piritramid	CT scan	Yes	Same side	152/96 (4)
WU-01	Yes (4)	Pethidine fentanyl	CT scan	No (nodulectomy)	CL side	140/85 (0)
SE-01	Yes (1)	None	None	Yes	CL side	127/78 (0)
SE-02	Yes (1)	None	None	Yes	CL side	122/79 (0)
SE-03	Yes (1)	None	None	No	N.A.	117/70 (3)
SE-04	Yes (1)	None	None	Yes	CL side	126/82 (1)
SE-05	Yes (1)	None	CT scan	No	N.A.	120/68 (2)
TO-01	Yes (3)	Morphine paracetamol	CT scan	No (nodulectomy)	CL side	135/85 (0)
VE-01	Yes (4)	Tramadol	CT and Scinti scan	No	N.A.	120/80 (1)
All	1.9±1.3					

**Table 2. Outcome parameters after adrenal haemorrhage.**

\*Minor asymptomatic extravasation of contrast was seen at the time of AVS and further imaging was not considered clinically indicated.

SBP = systolic blood pressure; DBP = diastolic blood pressure; CT = computed tomography; N.A. = not applicable; AVS = adrenal vein sampling; ADX = adrenalectomy.