Reduction of Radiation Exposure in Adrenal Vein Sampling: Impact of the Rapid Cortisol Assay

Reduktion der Strahlenbelastung bei der selektiven Nebennierenvenenblutentnahme: Einfluss des Kortison-Schnelltests

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ZUSAMMENFASSUNG
Ziel Bestimmung der Strahlenbelastung bei der selektiven Nebennierenvenenblutentnahme und deren Reduktion durch die Einführung des Kortison-Schnelltests sowie durch Modifikation des Probentnahmeprotokolls.


Schlussfolgerung Bei gleichzeitig steigenden technischen Erfolgsraten konnte die prozedurale Strahlenbelastung der selektiven Nebennierenvenenblutentnahme durch die Einführung des Kortison-Schnelltests deutlich verringert werden. Die zusätzliche Abnahme aus den Nierenvenen bot keinen diagnostischen Mehrwert in der Subtypbeurteilung des primären Hyperaldosteronismus, wobei durch eine Reduktion
Introduction

Adrenal vein sampling is a minimally invasive diagnostic procedure that represents an important step in subtype determination in patients with confirmed primary aldosteronism [1, 2]. Since its results have major impact on the further therapy strategy, adrenal vein sampling represents the gold standard in this scenario and is increasingly requested by endocrinologists. Since the procedure is technically demanding, both duration of adrenal vein sampling as well as intraprocedural radiation exposure have been shown to be notably high. In addition, a high variability between institutions that perform the procedure has been demonstrated [3–5].

Among other factors, this may be due to the lack of standardization of the sampling protocol and interpretation criteria [6].

Rapid cortisol assay is an intraprocedural test, whose benefits regarding procedural success rates have already been reported [7–9]. To date, there is only one study addressing the influence of the rapid cortisol assay on radiation exposure associated with adrenal vein sampling [10]. At the same time, data comparing different sampling protocols with special regard to radiation exposure, possibly leading to an optimization of the sequence, are not yet available.

To address the need for more data, the aim of this study was to analyze the impact of the rapid cortisol assay and a modified sampling protocol on radiation exposure.
Adrenal vein sampling procedure

Adrenal vein sampling procedures were performed by the same operator and carried out in our local angiography suite equipped with a state-of-the-art flat-panel detector C-arm angiographic system (Axiom Artis, Siemens AG, Healthcare Sector, Forchheim, Germany) including dedicated low-dose settings and collimation filters for the acquisition of fluoroscopic, radiographic, and DSA images (CARE Body, Siemens AG, Healthcare Sector, Forchheim, Germany). The parameters were: Tube potential 70 kVp, body-weight-adapted tube current setting ranging from 160 to 465 mA, 42 cm field of view, standardized system dose 0.36 μGy per pulse, pulse rate of 7.5 pulses per second, DSA frame rate of 2 frames per second, and variable and automatically adjusted pre-filtering ranging from 0.2 to 0.9 mm during fluoroscopy and from 0.0 to 0.9 mm during digital acquisition (referring to the absorption of the patient entrance dose along the path of the X-ray beam through the patient).

During the study period, changes to the systems’ algorithms regarding enhanced image quality (CLEAR features) have not been performed. Concerning radiation reduction tools, the following alterations have been made within the study period: CARE vision module in March 2010, and CARE monitor/guard in April 2017.

Considering the circadian rhythm of the endocrine system, sampling was usually performed in the morning. With all patients under local anesthesia, all adrenal vein sampling procedures were conducted via an antegrade right common femoral vein approach as a sequential sampling without ACTH stimulation. After introducing a 5-F sheath (Radifocus or Destination RDC, Terumo, Tokyo), different hydrophilic catheters as well as a 0.035” guidewire (Radifocus, Terumo, Tokyo) were used to catheterize the respective target vessel according to the protocols mentioned above. For sampling within the lower and upper IVC, a pigtail catheter (Angiodynamics, Queensbury, NY) was chosen. For sampling of the left adrenal vein, a Cobra-shaped catheter (5-F, C2, Boston Scientific, Natick, MA) was used up to a determined level of the orifice of the left renal vein and later exchanged for a catheter with a straight configuration (4-F, Glidecath, Terumo Tokyo). For sampling of the right adrenal vein, reverse-shaped selective catheters (5-F, Mikaelsson or 5-F VS2, Boston Scientific) were selected. In cases of sampling at the level of the left and right renal vein, a Cobra-shaped catheter (5-F, C2, Boston Scientific) was used.

Blood samples were collected in labelled tubes with EDTA. Tubes for the rapid cortisol assay were transferred to the endocrinology lab immediately after sampling. During the assessment of the rapid cortisol assay, the patients remained in the angiography room with the vascular sheath left in place, but the selective catheters were removed, to avoid thrombotic complications. When results of the assay indicated successful cannulation, the vascular sheath was removed and manual compression was applied, followed by a pressure bandage for hemostasis. In those cases, the assay revealed unsuccessful sampling. A second attempt at adrenal vein catheterization was performed.

In order to determine successful cannulation of the adrenal veins, the selectivity index was calculated as the ratio between cortisol concentrations from the sample of the supposed adrenal vein and a sample from the IVC. Sampling was considered as a primary technical success when bilaterally the selectivity index resulted in ≥ 2 [11]. For assessment of the lateralization of primary
Aldosteronism, the lateralization index was calculated as the ratio between the aldosterone-cortisol ratio of the dominant adrenal vein by the aldosterone-cortisol ratio of the non-dominant side. A unilateral source of primary aldosteronism was considered when the lateralization index resulted in $\geq 4$ [12, 13]. A sampling was regarded as a secondary technical success in those cases in which first selective catheterization was insufficient, but a second resampling yielded reliable cortisol values.

**Laboratory measurement**

Quantitative measurement of cortisol, including the rapid cortisol assay, was performed with a solid-phase competitive chemiluminescent enzyme immunoassay (IMMULITE 2000, Siemens Health-care, Erlangen, Germany). Until September 2014, serum aldosterone was determined by Coat-a-Count radioimmunoassay (RIA, Siemens). Starting in October 2014 serum aldosterone was analyzed – after a comprehensive cross-validation – by an automated chemiluminescence immunoassay (CLIA, ISYS, Immuno Diagnostic Systems).

**Data evaluation and endpoint definition**

Radiologic records and patient charts were reviewed by two authors together to extract information about the procedural radiation data and the technical success as the primary and secondary endpoints of the procedure. Patient and procedure...
data were retrieved from the department’s registry and the medical record system.

The primary endpoint of our study was the procedural radiation data including fluoroscopy time (min) and dose area product (Gy*cm²), which are routinely recorded during the intervention by the system’s radiation dosimeter. The dose area product is the cumulative radiation dose to which a patient is exposed. Furthermore, the effective dose (mSv), representing the estimation of stochastic risk related to radiation exposure, was calculated. The effective dose, which cannot be measured directly, is commonly calculated by the multiplication of dose area product with a suitable conversion coefficient (CC), depending on the area that is exposed to X-rays \( \text{ED} = \text{CC} \times \text{DAP} \) \cite{14, 15}. In this study, a CC of 0.21 mSv per Gy*cm² was used as previously described, leading to an estimated calculation of ED as follows:

\[
\text{Effective dose (mSv)} = \text{dose area product (Gy*cm²)} \times 0.21 \text{ (mSv/Gy*cm²)} \ 
\]

As secondary endpoints, technical success, correlation of the aldosterone-cortisol ratio between the adrenal and renal veins, and in cases of technical success, lateralization, and concordance with cross-sectional imaging, were investigated. In this context, overall technical success was defined as the diagnostic outcome of primary technical success and secondary technical success after resampling.

### Statistical analysis

Descriptive data were presented as means ± standard deviation for normally distributed variables or medians with ranges for non-normalized variables, if appropriate. Categorical data were expressed as counts and percentages with \( n(\% \) ). With regard to the assessment of normality, the Anderson-Darling test was used, rejecting the hypothesis of normality when the \( p \)-value is less or equal to 0.05. The Mann-Whitney U test and Student’s \( t \)-test were used for comparison of the described subgroups. Correlation analysis of ordinal and metrical data was performed with the test according to Spearman for non-normalized variables. For all evaluations, a \( p \)-value less than 0.05 was considered to indicate significant differences. Statistical analysis and the evaluation of the data were performed with a specialized computer algorithm (Microsoft Excel V1908 and RStudio 1.2.5033).

### Results

Patient characteristics and procedural data of the entire study cohort are presented in Table 1. In total, data of 151 patients and adrenal vein sampling procedures were evaluated. The overall technical success was 82.78%. The rapid cortisol test, which was introduced in March 2013, was applied in 130/151 cases (86.09%). Technical success was 33.33% in group I, 90.22% in group II, and 92.11% in group III. Based on the results of the rapid cortisol assay, revealing insufficient selective cannulation, a second sampling was performed in 27 cases. In 22 of those 27 cases (81.48%), secondary technical success was achieved by resampling. Within the study subgroups, the resampling, following negative results of the rapid cortisol assay, resulted in secondary technical success in 21.74% of the procedures in group II and in 5.23% in group III. In 2019, adrenal vein sampling protocols were revised and sampling from the renal veins was no longer performed. In total, renal vein sampling was part of the sampling protocol in 113/151 cases (74.83%).

The median dose area product for all procedures was 60.01 Gy*cm² (5.71–789.31). The median fluoroscopy time was 14.90 min, ranging from values between 3.27 and 80.90 min. The calculated median effective dose was 12.60 mSv (1.20–165.76). Statistically significant differences regarding radiation exposure parameters were found between all subgroups, in favor of subgroups II and III (Fig. 3). Differences in dose area product and fluoroscopy between groups I and II, characterized by the introduction of the rapid assay, were statistically significant with a reduction in dose area product of 57.94% (\( p < 0.001 \)) and fluoroscopy time of 40.48% (\( p = 0.026 \)). Excluding renal vein sampling from the protocol resulted in highly significant differences of

### Table 1 Patient and procedural data.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>52.85 ± 10.62</td>
</tr>
<tr>
<td>Male/female ratio</td>
<td>86:65</td>
</tr>
<tr>
<td>Median BMI (kg/m²)</td>
<td>29.03 (17.60–51.28)</td>
</tr>
<tr>
<td>BMI %</td>
<td>n</td>
</tr>
<tr>
<td>Overall procedures (n)</td>
<td>151</td>
</tr>
<tr>
<td>Overall technical success (%)</td>
<td>82.78 125/151</td>
</tr>
<tr>
<td>Group I</td>
<td>33.33 7/21</td>
</tr>
<tr>
<td>Group II</td>
<td>90.22 83/92</td>
</tr>
<tr>
<td>Group III</td>
<td>92.11 35/38</td>
</tr>
<tr>
<td>RCA (%)</td>
<td>86.09 130/151</td>
</tr>
<tr>
<td>Resampling (n)</td>
<td>17.88 27/151</td>
</tr>
<tr>
<td>Success after resampling (n)</td>
<td>81.48 22/27</td>
</tr>
<tr>
<td>Renal vein sampling</td>
<td>74.83 113/151</td>
</tr>
<tr>
<td>Overall median DAP (Gy*cm²)</td>
<td>60.01 (5.71–789.31)</td>
</tr>
<tr>
<td>Overall median FT (min)</td>
<td>14.90 (3.27–80.90)</td>
</tr>
<tr>
<td>Overall median ED (mSv)</td>
<td>12.60 (1.20–165.76)</td>
</tr>
<tr>
<td>Right-sided lateralization</td>
<td>26.40 33/125</td>
</tr>
<tr>
<td>Left-sided lateralization</td>
<td>33.60 42/125</td>
</tr>
<tr>
<td>No lateralization</td>
<td>40.00 50/125</td>
</tr>
<tr>
<td>Lateralization concordant to imaging</td>
<td>72.80 91/125</td>
</tr>
<tr>
<td>No concordance</td>
<td>24.20 34/125</td>
</tr>
</tbody>
</table>

BMI = body mass index; RCA = rapid cortisol assay; DAP = dose area product; FT = fluoroscopy time; ED = effective dose.

\[ \text{BMI} = \text{body mass index; RCA} = \text{rapid cortisol assay, DAP} = \text{dose area product; FT} = \text{fluoroscopy time; ED} = \text{effective dose.} \]
radiation exposure in groups II and III (p < 0.001 for both dose area product and fluoroscopy time) with a dose area product reduction of 40.44% and fluoroscopy time reduction of 40.47%. Corresponding results are illustrated in Table 2.

Analysis of correlation between a patient’s sex and radiation exposure resulted in significantly lower values of dose area product in female patients (88.00 vs. 38.82 Gy*cm², p < 0.001), whereas fluoroscopy time showed minor, but no statistically significant reduction in female patients (15.44 vs. 14.60 min, p = 0.256). A significant correlation between patient age and radiation exposure was not found. In this context, a rho-value of 0.066 (p = 0.420) was calculated for the dose area product and a rho-value of 0.043 (p = 0.570) was determined for fluoroscopy time. Resampling significantly increased radiation exposure with a median dose area product of 118.11 vs. 51.74 Gy*cm² (p < 0.001) and a median fluoroscopy time of 28.70 vs. 12.48 min (p < 0.001). Dose area product and fluoroscopy time showed a strong correlation (rho-value = 0.601; p < 0.001).

The median body mass index (BMI) of the whole patient cohort was 29.03 kg/m² (range 17.60–51.28) and revealed no significant differences between male and female patients (29.27 vs. 28.67; p = 0.107). However, bodyweight between male and female patients differed significantly (95 vs. 77 kg; p < 0.001) as well as body height (179.50 vs. 166.00; p < 0.001). Differences in median BMI between the subgroups were also not significant (p₁₂ = 0.509; p₂₃ = 0.279; p₁₃ = 0.887). However, a significant positive correlation between BMI and dose area product could be detected (rho-value 0.502; p < 0.001). In contrast, a relevant correlation between a patient’s BMI and fluoroscopy time was not found (rho-value –0.003; p = 0.399). A comparison of obese patients (BMI ≥ 30) and patients with a BMI < 30 resulted in highly significant differences in dose area product (112.70 vs. 46.55 Gy*cm²; p < 0.001), while a significant difference in fluoroscopy time could not be found (15.44 vs. 12.83 min; p = 0.592).

Technical success failed due to unsuccessful sampling on the right side in 13 cases, on the left side in four cases, and bilaterally.

Table 2 Results of subgroup analysis regarding radiation exposure.

<table>
<thead>
<tr>
<th>group</th>
<th>n</th>
<th>%</th>
<th>age (years)</th>
<th>BMI (kg/m²)</th>
<th>DAP (Gy*cm²)</th>
<th>FT (min)</th>
<th>ED (mSv)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>21</td>
<td>13.91</td>
<td>48.90 ± 9.29</td>
<td>29.67 (18.44–42.87)</td>
<td>146.02 (9.15–789.31)</td>
<td>25.20 (4.50–39.40)</td>
<td>30.66 (1.92–165.76)</td>
</tr>
<tr>
<td>II</td>
<td>92</td>
<td>60.93</td>
<td>53.41 ± 10.07</td>
<td>28.76 (18.52–48.96)</td>
<td>61.42 (15.04–481.08)</td>
<td>15.00 (4.00–80.90)</td>
<td>12.90 (3.16–101.03)</td>
</tr>
<tr>
<td>III</td>
<td>38</td>
<td>25.17</td>
<td>53.68 ± 12.28</td>
<td>29.91 (17.60–51.28)</td>
<td>36.58 (5.71–413.76)</td>
<td>8.93 (3.27–75.20)</td>
<td>7.86 (1.20–86.89)</td>
</tr>
</tbody>
</table>

Group I: Without RCA, including renal vein sampling; group II: with RCA, including renal vein sampling; group III: with RCA, without renal vein sampling. BMI = body mass index; DAP = dose area product; FT = fluoroscopy time; ED = effective dose.

Abb. 3 Dosis-Flächen-Produkt (Gy*cm²) und Durchleuchtungszeit (min) der 3 Studiengruppen. Gruppe I: ohne Kortison-Schnelltest, einschließlich der Abnahme aus den Nierenvenen; Gruppe II: mit Kortison-Schnelltest, einschließlich der Abnahme aus den Nierenvenen; Gruppe III: mit Kortison-Schnelltest, ohne Abnahme aus den Nierenvenen.

Tab. 2 Ergebnisse der Subgruppenanalyse in Bezug auf die Strahlenbelastung.

Fig. 3 Dose area product (Gy*cm²) and fluoroscopy time (min) of the three study subgroups. Group I: Without the rapid cortisol assay, including renal vein sampling; group II: with rapid cortisol assay, including renal vein sampling; group III: with rapid cortisol assay, without renal vein sampling.

Fig. 4 Technical success failed due to unsuccessful sampling on the right side in 13 cases, on the left side in four cases, and bilaterally.
in nine cases. Results of the Chi-Square Test showed a strong correlation between the side of sampling and the technical success in terms of a significantly higher rate of unsuccessful sampling due to failure on the right side (p < 0.001). Lateralization of aldosterone excess was confirmed in 75 of 125 cases (60.00 %) and revealed a left-sided hormone excess in 42 (33.60 %) and right-sided in 33 (26.40 %) technically successful procedures. In 50 cases (40.00 %), adrenal vein sampling did not reveal unilateral hypersecretion with subsequent diagnosis of bilateral adrenal hyperplasia.

In 91/125 cases (72.80 %), analysis of preinterventional CT and MRI was concordant with adrenal vein sampling with an adrenal mass on the side of hormone excess or no adenoma in cases of bilateral aldosteronism. In 16 cases (12.80 %), the presence of a unilateral adenoma on imaging was not associated with the confirmed diagnosis of unilateral aldosterone overproduction by successful catheterization. One case resulted in lateralization on the left side, while adenoma was detected on the contralateral side, which was confirmed histologically. In 17 cases (13.60 %), unilateral origin of aldosterone excess was found, although an adenoma had not been identified on MRI or CT (Fig. 5).

Sampling from the renal veins was performed in 113 cases (74.83 %). Spearman’s correlation analysis revealed a moderate association between aldosterone-cortisol values of the left adrenal vein and the left renal vein (r = 0.43; p < 0.05). In contrast, the correlation of the renal and adrenal aldosterone-cortisol ratio on
Discussion

Fluoroscopy-guided abdominal interventions like adrenal vein sampling are generally considered to be radiation-intensive procedures [3, 17]. The importance of optimizing radiation exposure in adrenal vein sampling is additionally emphasized by the fact that patients undergoing this procedure are usually younger than those receiving other endovascular procedures. Therefore, the mean age of the patients included in this study was 52.9 years.

In this retrospective study, we evaluated the impact of the rapid cortisol assay as well as the modification of the adrenal vein sampling protocol and its impact on radiation exposure.

Due to the fact that all procedures were performed by the same interventional radiologist, biases due to differing preferences in procedure strategy and protocol settings did not play a major role, even if the other staff members changed over time. Furthermore, the same flat-panel detector C-arm angiography system was used during the whole study period, thus hardware-dependent influences can be neglected. The number of included procedures is a strength of the study, which is attributed to the fact that our hospital is one of the national referral centers for primary aldosteronism.

Implementation of the rapid cortisol test for intraprocedural verification of correct sampling locations resulted in a significant reduction of radiation doses. Those results are consistent with one study, addressing this special topic and proving increased success rates while at the same time minimizing radiation exposure during adrenal vein sampling [10]. Presumably, this is caused by the increased diagnostic confidence gained from the peri-procedural rapid cortisol assay. In adrenal vein sampling without the test, the interventionalist tends to use longer fluoroscopy times and more frequent acquisition of DSA series in order to verify the

the right side proved to be minor and not significant ($r = 0.16; p = 0.172$). Over the study period of 11 years, a successive reduction of dose area product and fluoroscopy time could be observed, while at the same time the technical success rate increased (Fig. 6).
correct sampling site. As a powerful tool, the rapid cortisol assay offered prompt feedback concerning the technical success of procedures and made it possible to bail out in cases in which the first attempt at diagnostic sampling failed. Therefore, repeated procedures may be avoided, which will inevitably lead to a reduction of costs, a decrease of procedure-related risks, accelerated diagnostics, and a faster initiation of therapy, although those aspects were not the subject of the presented study. The certainty of being able to perform repeated sampling during the same procedure in the event of an inadequate result may thus have a relevant impact on the procedural strategy of interventional radiologists.

In our study collective, resampling was performed in 27 of 151 procedures, with secondary technical success in 22 procedures (81.48 %), increasing the overall technical success by 14.57 %. Even though execution of resampling was associated with increased radiation, this additional radiation exposure is lower than the doses associated with a repeated procedure and is therefore justifiable.

A previously performed multicenter study analyzed the radiation doses during adrenal vein sampling procedures in different centers and revealed a high variability between the performing institutions [3]. In this context, the dose area product of the respective centers ranged between 16 and 147 Gy cm², fluoroscopy time between 3.2 and 29 min and ED between 16 and 27 mSv. Taking those results as a reference, the initial radiation exposure values in our study collective (Group I) are comparable to those with the highest dose area product, fluoroscopy time, and effective dose, whereas, after implementing all described revisions of the protocol of the procedures (Group III), radiation dose parameters similar to those in the lower third of the evaluated parameters were achieved.

In contrast to previous studies, we additionally evaluated the habitus of the patients that underwent adrenal vein sampling. The radiation dose is highly influenced by the patient’s physical constitution with higher radiation doses in obese patients [18, 19]. Accordingly, our results revealed a significant correlation between the patient’s BMI and procedural dose area product. Furthermore, significant differences in dose area product were found between patients with obesity and those without. Influences on the subgroup results based on unequal BMI values could be excluded. Furthermore, the higher dose area product in overweight patients was not attributed to longer fluoroscopy times. Interestingly, with comparable fluoroscopy times, dose area product values between male and female patients were significantly different. However, the body height and weight of the male patients was significantly higher, thus not only BMI but also patient size might be predictors for the resulting dose area product [20].

As a further endpoint of the presented study, procedural success rates increased after implementation of the rapid cortisol assay. This fact shows high concordance with other previously performed studies, proving an increase in technical success, especially in centers with only little experience with adrenal vein sampling. With a remarkably high number of resamplings, Betz et al. [21] reported an improvement of the technical success rate of 30 %. In a moderate-sized patient collective, Rossi et al. [8] achieved a technical success rate of 92 % after implementation of the assay compared to a historical series without the rapid cortisol assay with a success rate of 76 %. Another study reported an increase of the success rate of 26 %, comparing 30 conventional adrenal vein sampling procedures with 30 procedures after the establishment of the rapid cortisol assay [7].

Beside the rapid cortisol assay, a significant reduction in radiation dose was observed after revising the sampling protocol in terms of omitting sampling from the renal veins. Prior to this, renal vein sampling had been performed, since venous drainage of adrenal glands had also been described for the right side, albeit to a lesser extent than on the left [22]. Various investigations have been performed in the past with the goal of assessing incomplete, but complementary adrenal vein sampling data with special regard to a reliable determination of the primary aldosteronism subtype. In this context, one secondary endpoint of the presented study was evaluating the value of additional blood sampling from the renal veins. Hypothetically, in the case of a strong correlation of aldosterone and cortisol levels in the renal and adrenal vein, the technically less challenging blood sampling from the renal veins could serve as an alternative in cases of unsuccessful adrenal sampling. Our data revealed a moderate correlation between aldosterone and cortisol quotients on the left but only a poor association on the right side. This result seems to be reasonable and consistent based on anatomical aspects of the adrenal veins. The left adrenal vein directly drains into the ipsilateral renal vein. Therefore, the level of adrenocortical hormones from samples of the renal vein can be expected to be higher due to fewer dilution effects. On the right side, a direct anatomical connection between the renal and adrenal vein does not exist. Therefore, results are distinctly affected by dilution. Even if the finding or exclusion of pathologically elevated aldosterone levels on the left side might help to predict the primary aldosteronism subtype, results of other studies indicated inadequate sensitivity of incomplete adrenal vein sampling data in terms of identifying patients suitable for surgery [23]. We, therefore, consider sampling from the renal veins to be non-diagnostic and neglectable.

In our study setting, the rapid cortisol assay was performed in the hospital’s laboratory, whereas other institutions are already able to carry out the assay in the local angiography suite with a point-of-care system [9]. This might be certainly advantageous because of the potentially faster processes, direct feedback, and the possibly reduced risk of errors in sample identification. Therefore, such a setting seems to be preferable in centers where adrenal vein samplings are frequently performed.

With almost a third of the successful procedures leading to discordant results with CT and MRI, our results revealed similar unreliability in subtype diagnostics based on cross-sectional imaging alone, when compared to other studies [24, 25]. In this scenario, the failed assessment of a hormonally inactive adenoma as the source of hormonal excess may lead to unnecessary surgery or, in the worst case, to adrenalectomy on the incorrect side. On the other hand, an unproven unilateral subtype of primary aldosteronism based on CT and MRI might be insufficiently treated with mineralocorticoid antagonist therapy, frequently failing to normalize blood pressure [26].

The lack of standardization of data interpretation and solid diagnostic criteria, especially due to different SI and L1 values,
may lead to different results in the same scenarios and thus constitutes a limitation regarding the procedural diagnostic reliability [27, 28]. This restriction must be taken into account when interpreting results of adrenal vein sampling. It emphasizes the importance of making the final diagnosis of primary aldosteronism subtype considering all available individual findings and aspects.

The limitations of this study include the retrospective, single-center, and non-randomized study design. Moreover, the impact of the rapid cortisol assay on the technical success rate as well as radiation dose could be overestimated and partially be the well-known side effect of the learning curve of interventionists [29]. Nevertheless, Jakobsson et al. [30] found a plateau of satisfactory results after performing approximately 36 interventions and those results are likely to be transferable with respect to radiation protection habits. At the time of the study start, the interventional radiologist performing the procedure had 12 years of experience with interventional procedures, including adrenal vein sampling. This might also be reflected by the timeline representing the technical success over the years (Fig. 6), proving a plateau of technical success at 80% reached in 2012, which was again slightly improved after the introduction of the cortisol assay. Radiation exposure parameters, on the other hand, revealed a successive increase within the first study years, but significantly reduced after implementation of the rapid cortisol assay. Therefore, the overall influence of the learning curve on radiation exposure was minor as compared to the implementation of the rapid cortisol assay.

Furthermore, alterations of the image-quality and dose-saving tools provided by the manufacturer might have a relevant impact on radiation dose, regardless of the procedural protocol [31]. Nevertheless, we retrospectively assessed that during the study period significant changes in the dose reduction portfolio have not been performed. The only feature that was added during the study period and that could possibly have an influence on radiation exposure was the CARE vision module, which was implemented in March 2010. However, a significant change in radiation doses was not found during this period. Since this alteration had been performed at the start of the study period, we do not expect a relevant impact on the analyzed data.

Another limitation is represented by the calculation of the effective dose. As a quantitative parameter for the stochastic risk associated with radiation exposure, it cannot be measured directly but is calculated by multiplication of the dose area product with the appropriate conversion coefficients, considering factors like tube voltage, field position, filtration, and patient characteristics [32, 33]. In this study, effective dose values were calculated using a single correlation coefficient suggested by the literature, considering neither the patient’s gender nor bodyweight [16]. We are aware that this can only serve as an approximate estimation. Nevertheless, since this study addresses the differences in radiation exposure between the different subgroups rather than the determination of absolute values, this simplified process seems to be justified in our opinion.

In conclusion, implementation of the rapid cortisol assay in adrenal vein sampling leads to a significant reduction of radiation exposure in patients while at the same time increasing the procedural technical success and preventing reintervention. Since additional sampling from the renal veins does not offer additional diagnostic value, these sampling locations were omitted which led to a further radiation reduction.

**Conflict of Interest**

The authors declare that they have no conflict of interest.

**References**


