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Research article

Can computed tomography volumetry of the renal cortex replace MAG3-scintigraphy in all patients for determining split renal function?

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ABSTRACT

Objectives: The current gold standard for determination of split renal function (SRF) is Tc-99m-mercapto-acetyltriglycin (MAG3) scintigraphy. Initial studies comparing MAG3-scintigraphy and CT-based renal cortex volumetry (RCV) for calculation of SRF have shown similar results in highly selected patient collectives with normal renal function (i.e. living kidney donors). This study aims to compare MAG3-scintigraphy and CT-RCV within a large unselected patient collective including patients with impaired renal function.

Materials and methods: For this assessment, 279 datasets (131 men, 148 women; mean age: 54.2 ± 12.9 years, range: 24–84 years) of patients who underwent MAG3-scintigraphy and contrast-enhanced abdominal CT within two weeks were retrospectively analyzed. Two independent readers assessed the CT-RCV in all CT datasets using a semi-automated volumetry tool. The MAG3-scintigraphy and CT-RCV methods were compared, stratified for the eGFR. Statistical analysis included descriptive statistics as well as inter- observer agreement.

Results: The absolute mean difference between the percentage contribution of the left and the right kidneys in total MAG3-clearance was 8.6%. Independent of eGFR, an overall sufficient agreement between both methods was established in all patients. A relatively small, tolerable systemic error resulted in an underestimation (max. 2%) of the left renal contribution to overall RCV.

Conclusion: The results demonstrate that CT-RCV is a potential clinical replacement for MAG3-scintigraphy for calculation of SRF: CT-RCV demonstrates clinically tolerable differences with MAG3-scintigraphy, independent of patient eGFR. The relative complexity of the RCV method utilized is a potential limitation and may have contributed to the acceptable but only fair to moderate level of intra-reader reliability.

1. Introduction

Routine serum creatinine (Cr) values or calculated estimated glomerular filtration rate (GFR) provide information on overall renal function in addition to measured GFR. However, these laboratory values do not allow for assessment of the individual function of each kidney. However, for a spectrum of clinical situations, diseases, and therapeutic procedures, it is mandatory to obtain detailed information about renal function of the kidneys individually [1,2]. For example, such information is critical in the pre-operative evaluation of living kidney donors to minimize the risk of subsequent end-stage renal disease (ESRD). In order to avoid explanting the dominant kidney of a renal donor, determination of the so-called split-renal function (SRF) is required [1,3,4].

Over the last few decades, the gold standard for determination of SRF has become dynamic scintirenography, most commonly using the tracer 99mTc-mercaptoacetyltriglycine (MAG3-scintigraphy). The pharmacokinetics of MAG3 are preferable for dynamic imaging compared to Tc-99m-diethylene triamine pentaacetic acid (DTPA) or Tc-99m-dimercaptosuccinic acid (DMSA) due to its ability to assess renal clearance and excretion [1]. Although a well-established technique, MAG3-scintigraphy does require careful consideration of variables

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related to the hardware and software utilized for acquisition [5]. Importantly, the estimation or measurement of GFR is typically performed using markers eliminated primarily by glomerular filtration, whereas MAG3 is exclusively secreted by the tubular system (in contrast to DTPA), thus providing different information regarding kidney function. Consequently, the predictive value of SRF has been questioned, resulting in the discontinuation of its use at several transplant centers [6]. Another limitation of MAG3-scintigraphy is the lack of morphological information provided, particularly with respect to vascular anatomy. MAG3-scintigraphy is thus often combined with contrast-enhanced computed tomography (CT) for pre-operative donor transplant evaluation.

Due to its pre-existing use in transplant donors, CT has been evaluated for functional assessment of the kidneys over the last few years. Several different CT-based methods utilizing either renal attenuation or morphological information to determine SRF have been introduced. The reported correlations between such approaches and nuclear renography SRF vary widely from 0.43–0.98. Furthermore, the available CT-based solutions [6–10] are heterogeneous with respect to complexity, post-procedure processing requirements, and inter-observer reliability. The availability of reproducible, simple, fast, and accurate methods of computation, including (semi-) automated techniques, would thus be beneficial. Semi-automated segmentation tools are now well-established for the assessment of lung nodules, liver lesions, lymph node metastases, kidney volumetry in polycystic kidney disease, and cardiac segmentation, demonstrating high reproducibility and accuracy relative to manual measurements [11–15].

The most promising techniques for CT-based calculation of SRF in the literature are: (1) the modified ellipsoid volume [MELV], a simple and fast measurement based on renal diameters on maximum-intensity-projections and calculation of renal volume via the rotation ellipsoid formula; (2) smart region of interest [ROI] volumetry, a more complex semi-automated tool-based calculation of the whole kidney volume; and (3) renal cortex volumetry (RCV) which is similar to (2) but even more complex as it examines only the renal cortex. The last approach (3) has demonstrated the most accurate results in evaluation of pre-donation SRF in a cohort of healthy, highly-selected, living kidney donors, enabling reliable long-term prediction of the donor renal function following explantation [4]. Based on these findings, the current study aims to determine (1) the equivalency of renal cortex volumetry (RCV) and MAG3-scintigraphy in different stages of (uni- and bilateral) renal functional impairment, (2) the inter-reader agreement with RCV, and (3) the correlation between inter-reader agreement and renal function.

2. Materials and methods

2.1. Compliance with ethical standards

The local institutional review board approved this retrospective study and waived the requirement for informed consent. The local IRB is the ethic committee of the medical faculty of the University of Cologne (the internal reference number of the study: 16-288). Furthermore, the authors state, that the methods of this study were carried out in accordance with the relevant guidelines and regulations.

2.2. Study population

One faculty member of the nuclear medicine department (M.S.) searched radiology information system (RIS) for patients referred to nuclear medicine for renal MAG3-scintigraphy from 01/2010 to 06/2015. One radiologist (C.H.) cross referenced this list with the radiology RIS to identify patients who had also undergone contrast-enhanced, biphasic CT of the abdomen within 2 weeks of scintigraphy. Additional clinical data including the serum creatinine (CR) and estimated glomerular filtration rate (GFR) at the time of CT were recorded from the local clinical information system. The data were all sampled by the local Institute for Clinical Chemistry. The only study inclusion criteria was a patient age > 18 years.

2.3. Computed tomography

All CT examinations were conducted using a state-of-the art 64 or 128 slice CT scanner (Brilliance 64 or iCT 256; Philips Healthcare, Best, Netherlands). Patients were scanned head-first and supine. A body-weight adapted volume of a non-ionic, iodinated contrast media (Accupaque 350 mg/ml, GE Healthcare; Little Chalfort, UK) was injected intravenously via a peripheral vein utilizing an automated injection system (MEDRAD, Bayer Healthcare, Berlin, Germany) at a mean flow rate of approximately 3.5 ml/s followed by a saline flush. For dose optimization, the standard clinical dose modulation algorithm was activated (DoseRight 3D-DOM or Z-DOM). A bolus tracking technique was utilized to begin image acquisition with a delay of 30 s and 70 s after reaching threshold values of 100 HU for late arterial phase and venous phase imaging, respectively. The late arterial and venous phase images were reconstructed at a slice thickness of 2 mm with a standard soft tissue kernel.

2.4. CT image analysis

One board-certified radiologist (C.H.) with an experience of 6 years in abdominal imaging and one doctoral candidate (M.M.) analyzed all CT-datasets in a blinded and independent manner after a consensus training session with 5 patient datasets. RCV was performed on the late arterial-phase CT images using the semi-automatic volumetric tool of the clinical DICOM viewer (ISP 8.0, Philips Healthcare, Best, Netherlands). This tool is based on a 3 dimensional, growing-region-algorithm with preset density threshold values. The CT dataset is automatically resampled and shown in 3 dimensions. The readers set the point of origin in all three dimensions in the renal cortex and manually adjusted the tool-based density recognition of the cortex in all planes. Structures altering the cortical morphology such as renal cysts were manually excluded from volumetry. Finally, the software calculated the renal volume for each kidney separately. An example image is given in Fig. 1. For determination of intra-reader agreement, 10 patients were randomly chosen by a radiologist who was not involved in the reading (S.H.) and presented to the two readers in a second session 4 weeks after the initial evaluation.

2.5. MAG3-scintigraphy and analysis

Patients received 500 ml of water for oral hydration and were scanned supine with the gamma camera below the table. On average, 100 MBq of Tc-99m-MAG (3 mercaptoacetyltriglycine, MAG-3 ROTOP, Dresden, Germany) was injected intravenously. A three-phase dynamic acquisition protocol over 30–40 min was used beginning with 60 × 1-s frames followed by 24 × 5-s frames and 54 or 74 × 30-s frames. Typically, 20–40 mg of furosemide was injected 20 min following the start of the acquisition. The data were processed using standard post-processing software (Syngo, Siemens Healthineers, Erlangen, Germany). Clearance values were calculated using two blood samples drawn from a separate venous site at the end of the acquisition. Background-subtracted curves were generated for the whole kidneys for automatic calculation of multiple quantitative parameters. Relative uptake values were calculated based on the integral of renal counts in the region of interest 1.5–2.5 min after the bolus reached the kidneys.

2.6. Statistical analysis

Statistical analysis was performed by M.H. using SPSS Statistics (Version 22; IBM Corp., Armonk, NY, USA). Descriptive statistics are given as mean and standard deviations if not indicated otherwise. For