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Ultrasonographic renal volume measurements in early autosomal dominant polycystic disease: Comparison with CT-scan renal volume calculations

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Polycystic kidney disease; Volumetry; Ultrasonography; CT-scan

Abstract
Purpose: To investigate the correlation and concordance between the ellipsoid volume calculated by ultrasonography measurements (Vol3DUS) and the reference kidney volume measured by CT (VolTDM) in early autosomal dominant polycystic kidney disease (ADPKD).
Materials and methods: Prospective study of the correlation and concordance of renal volumes in 24 patients with early ADPKD (48 kidneys analysed separately), with calculation of Vol3DUS using the formula for an ellipsoid in three different manners and VolTDM measurement by manual contouring. Calculations of correlation coefficients (r) and coefficients of intra-class correlation (ICC) with confidence intervals at 95%.
Results: The US volume was strongly correlated with the CT volume by using the maximum width in a transverse section (r = 0.83) with a mean Vol3DUS = 692 ± 348 ml [180; 2069]. The most reproducible ultrasonography measurement was the height. When the kidney volume exceeded 800 ml, US underestimated the volume. However, the median error was −57.5 ml [−1090; 183] and 85% of the Vol3DUS calculated differed by more than 5% from the reference measurement.

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Conclusion: The correlation between the US calculated volumes and the CT volumes was strong. However, the median error with ellipsoid US volume was too high to detect a small renal variation in early ADPKD.

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Autosomal dominant polycystic kidney disease (ADPKD) is the most common genetic kidney disease with an incidence of 1/1000. Detected in the young adult, it is characterised by the presence of multiple kidney cysts associated with liver cysts and more rarely with cardiovascular anomalies [1]. Terminal kidney failure is the most serious complication and affects about 80% of the patients before the age of 70 [2]. In fact, the progressive growth of the cysts increases the total volume of the kidney and is accompanied by an alteration in the renal parenchyma. There seems to be a relationship between the renal volume and the glomerular filtration rate (GFR), the main biological marker for the progression of the disease [3]. In fact, the GFR remains stable until about the age of 50, thanks to the compensating ability of the healthy remaining renal parenchyma. However, as of a certain renal volume threshold, the GFR begins to decrease [3]. The new treatments [4,5] try to reduce the growth of cysts and are currently being assessed. They should present an increase in efficacy during the early stage in the evolution of the disease, before the onset of kidney failure (and therefore before the renal volume reaches this critical threshold) [6,7]. Therefore, the monitoring of the renal volume seems to be pertinent in the early assessment of the efficacy of these recent therapies [7–11]. To measure it, the recent studies have used MRI [10,12]. This expensive examination is of limited access and is not always possible (claustrophobia, pacemaker, high abdominal perimeter...). The CT-scan is also an exact technique [13] although it exposes the patient to the risks of iterative irradiation and possibly the injection of an iodine contrast product. The 2D ultrasound examination, more accessible and without any counter-indications, raises the problem of inter-observer and intra-observer variation [14,15] on the one hand and the approximation of the calculated volume on the other hand. The purpose of this prospective study is to compare the renal volumes calculated by ultrasonography with the reference renal volume measured by CT-scan, in order to determine the value of this technique in assessing the growth of renal volume in early ADPKD patients when their renal function is normal.

Materials and methods

This is a prospective single centre study on patients selected to participate in a therapeutic trial. The criteria for inclusion are:
- adult patients;
- with early autosomal dominant polycystic disease;
- with a normal renal function (defined by a glomerular filtration rate ≥ 60 ml/min), which corresponds to the beginning stage of the disease;
- having signed the French ethics committee-approved informed consent form.

Twenty-four patients were prospectively included over a period of 7 months. The patients were 25 to 58 years old with a mean of 42.2 ± 8 years [25; 58], comprising 16 women and eight men. Each patient underwent a 2D ultrasound examination and an abdominal CT-scan without injection at an interval of two months.

2D ultrasound measurements

The 2D ultrasound was carried out with an iU22 ultrasound machine (Philips US, Bothell, WA, USA) in composite harmonic mode with a wide band convex sound (C5–1; 1 to 5 MHz), using the “widescreen” mode that increases the sector studied. The different readings were taken by a single operator, three consecutive times, for each plane and each kidney (Fig. 1):
- H: maximum height of the kidney, measured in the coronal bivalve plane in widescreen mode;
- Dt1: maximum transverse width, measured in the coronal bivalve plane at the height of the kidney sinus;
- E: maximum thickness measured in the transverse plane;
- Dt2: Maximum transverse width, measured in the transverse plane;
- the kidney surface was measured in the coronal bivalve plane (CBP) and in the transverse plane (TP) by the ellipse technique by defining the four cardinal points.

The volume was calculated using the mean of each of the measurements obtained according to the ellipsoid formula: height × transverse width × thickness × π/6. Thereby, three different volumes were obtained according to the method to measure the transverse width:

\[
\text{Vol}3\text{DUS}_1: \frac{H \times E \times D_t_1 \times \pi}{6}
\]

\[
\text{Vol}3\text{DUS}_2: \frac{H \times E \times D_t_2 \times \pi}{6}
\]

\[
\text{Vol}3\text{DUS}_3: \frac{H \times E \times (D_t_1 + D_t_2)/2 \times \pi}{6}
\]

(transverse width = mean of two measurements)

The time to calculate the volume for a kidney was about 3 to 5 minutes.

CT measurements

The examinations were carried out without the injection of contrast product with a GE VCT LightSpeed scanner (Milwaukee, USA) by optimising the acquisition parameters to obtain a section thickness of 1.2 mm. The volume was calculated in double blind of the ultrasonography by an independent operator on an Advantage Windows 4.1 workstation (GE Advantage Windows, Milwaukee, USA). The volume of the kidneys was obtained in two different ways:
- from the calculation of the three widths of the kidney measured in the three planes obtained by
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Figure 1. Measurement of the renal volume by ultrasonography: a: diagram representing the techniques to measure the ultrasound widths; b: measurement of the height in the bivalve coronal plane in normal mode; c: measurement of the height in bivalve coronal plane in widescreen mode; d: measurement of the thickness and transverse width in the axial bivalve plane.

reformatting of the volume, by considering the kidney as a revolution ellipsoid (volume = height × transverse section × thickness × π/6). The three dimensions of the kidney were measured after reconstruction with a double obliquity (volTDMcal): the maximum height measured in the oblique coronal section, the transverse section measured in an axial bivalve plane, the thickness measured in an axial bivalve plane;

• from the reformatting in the coronal plane on joined reconstructed sections 3 mm thick, the outlines of the kidney designed manually with a “tissue outline” tool. The total renal volume was obtained automatically by the sum of the volume of the sections and corresponded to the reference volume (volTDMmes). The time to calculate the volume of each kidney varied from 10 to 20 min according to the size and the number of reconstructed sections.

The reproducibility of the ultrasound measurements and the concordance between the volumes calculated according the ellipsoid formula (by CT-scan and ultrasonography) and the reference volume by CT-scan were assessed using intra-class correlation (ICC) coefficients with the intervals of confidence at 95% (IC). Graphic representations by Bland and Altman were also carried out. The analysis was carried out with R software (http://www.r-project.org).

Results

Mean kidney volume

The volumes of each kidney were obtained for the 24 patients by ultrasonography and with CT-scan (a total of 48 kidney volumes). The mean reference volume (VolTDMmes) was 798 ± 511 ml [168; 2711].

Reproducibility of the ultrasonography measurements

The reproducibility of the ultrasonography measurements (different widths of the kidney and surfaces measured in the

Statistical analysis

Each kidney unit was considered independently.

The correlation between the volumes measured and calculated with the CT-scan and between the volumes calculated with ultrasonography was obtained by calculation of the correlation coefficient $r$.

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Table 1  Intra-class correlation coefficients assessing the concordance between the CT-scan volume measured and the different volumes calculated (CT-scan and ultrasonography).

<table>
<thead>
<tr>
<th>ICC</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>VolTDMcalc</td>
<td>0.97 [0.97–0.99]</td>
</tr>
<tr>
<td>Vol3DUS1</td>
<td>0.62 [0.44–0.82]</td>
</tr>
<tr>
<td>Vol3DUS2</td>
<td>0.83 [0.76–0.93]</td>
</tr>
<tr>
<td>Vol3DUS3</td>
<td>0.74 [0.61–0.88]</td>
</tr>
</tbody>
</table>

ICC: Intra-class correlation.

Correlation and concordance of the volume measurements

The kidney volumes calculated by the ellipsoid formula in TDM were correlated with the kidney volumes measured by tissue outline in TDM, with a correlation coefficient $r = 0.99$ (Fig. 2). The ICC coefficient between the kidney volumes calculated with the CT-scan and the reference volume was 0.97 [0.97; 0.99] (Table 1). The median error of the volume calculated with the CT-scan was $-41.5\, \text{ml} \, [-347.2; 320.3]$, corresponding to a mean percentage error of $-7\% \, [-28.2; 18.5]$ (Fig. 3).

Since there are several references to determine by ultrasonography a transverse width, we calculated ultrasound volumes with the ellipsoid formula according to different techniques to measure the transverse width. The best correlation with the reference volume was found by using the measurement of the widest transverse section in the axial plane with a vol3DUS2 mean of $692 \pm 348\, \text{ml} \, [180; 2069]$. The vol3DUS2 were correlated with the reference kidney volumes measured in TDM, with a lower correlation coefficient ($r = 0.86$) (Fig. 2). The ICC value was good, equal to 0.83 [0.76; 0.93] (Table 1). Nevertheless, with this method, the median deviation with respect to the reference was $-57.5\, \text{ml} \, [-1090; 183] \, \text{and 85}\% \, \text{of the measurements were erroneous by at least 5\% (Fig. 4).}$

Concordance between the volume and the surface in the bivalve planes and transverse planes

To determine the technique to monitor the kidney growth, we looked for the concordance between the surface of the section measured in the transverse plane or in the coronal bivalve plane and the kidney volume. The best concordance was obtained at the mean of the surface in the transverse plane with an ICC at 0.86 [0.76; 0.92]. These values are good but similar to those found for the volume.

Concordance of the width measurements in ultrasonography and TDM

To account for the insufficient concordance between the volumes calculated by ultrasonography and the volume measured with the CT-scan, it is possible to incriminate the measurement of the widths or the method to calculate the volume (ellipsoid formula). To solve this question, we studied the concordance between the widths measured by ultrasonography and those determined with the CT-scan. The ICC was determined for each measurement. The height was the measurement most concordant with an ICC between 0.80 [0.69; 0.87] and 0.82 [0.73; 0.90]. The graphs were carried out with a mean measured value (Fig. 4). The ICC of the measurements of the transverse widths and the thickness were inferior.

Figure 2. Comparison of the renal volumes calculated at the reference CT-scan renal volume by the calculation of the linear correlation coefficients $r$: a: graphic representation of the correlation of the renal volume calculated by CT-scan with the reference volume; b: graphic representation of the correlation of the renal volume calculated by ultrasonography (by means of the transverse width in their axial plane) with the reference volume.
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Figure 3. Comparison of the renal volume measured by CT-scan with the volume calculated by CT-scan: a: graphic representation by Bland and Altman. Median bias: $-41.5\text{ ml} \ [−347.2; 320.3]$; b: deviations of the volTDMcal with respect to the volTDMmes reference in percentage. Median deviation: $-7.5\% \ [−28.2; 18.5]$.

Discussion

In this study, the ultrasound measurements were made by the same operator trained for the different acquisitions carried out consecutively. The intra-observer concordance was very high. This high reproducibility is also attributed to the fact that the size of the kidneys was slightly greater. The measurement that presented the best reproducibility was that of the kidney height, as already mentioned in the literature [16] in a work on the inter-observer variation. It is necessary to underline the use of the "widescreen" mode that allows the height measured to be increased by 40% (+55 mm) at 5 cm depth and by 17% (+35 mm) at 10 cm depth. The variability of the ultrasonography measurements above all involves the inter-observer measurements, a parameter that we did not assess in our study [14,15]. With the increase in the size of the kidneys, the precision of the ultrasonography measurements decreases, accounting for a limit for

Figure 4. Comparison of the ultrasound measurements with the CT-scan measurements: a: comparison of the renal volume measured by CT-scan with the volume calculated by ultrasonography: graphic representation by Bland and Altman. Median bias: $-57.5\text{ ml} \ [-1090; 183]$. The deviation between the measurement calculated and the reference did not exceed $-5\%$ in 26 cases (54%) and equal or greater by 5%, in 15 cases (31%); b: comparison of the measurement of the ultrasonography height with that of the CT-scan. Graphic representation by Bland and Altman.
patients with voluminous polycystic disease where the kidney volumes may exceed 8000 litres. However, measurement of the kidney volume as a marker of the efficacy of a preventive treatment for the development of kidney failure in ADPKD should only involve patients with a low or moderate increase in kidney volume, at the initial stage of the disease.

There are no recommendations for the measurement of the transverse kidney width. It may be obtained with a longitudinal section or a transverse axial section. Our study assesses these two possibilities separately (as well as the mean of these two measurements). The best concordance between the ultrasonography volumes calculated and the reference volume determined by TDM was found using the measurement of the widest transverse width in the axial plane. We deduced that this was the measurement to promote.

As already demonstrated, in particular in the studies comparing the ultrasonography volumes calculated and those measured by MRI [16,17] or by CT-scan [18], we found a high correlation between the volume calculated by ultrasonography (using a measurement of the transverse width on a transverse section) and the reference tomodensitometry volume with an \( r = 0.86 \) and an ICC at 0.83 [0.76; 0.93]. Nevertheless, the median error of the ultrasonography calculation of the renal volume was 57.5 ml, exceeding the renal volume by over 5% in 85% of the cases. Analysis by sub-category did not reveal a significant difference for the kidneys where the volume was slightly increased (remaining under 750 ml) with less than 5% error in 78% of the cases (results not provided). In the CRISP study [6], the annual mean variation in total renal volume was 5.3 ± 3.9% for kidneys of mean volume 1060 ± 642 ml. In the same study, the annual variation in the renal volume in patients with ADPKD depended on the renal volume, with a mean annual growth of 25 ml for kidneys less than 500 ml (or about 4%) and 55 ml for kidneys between 750 and 1500 ml (or about 5%) [6]. A more recent study estimated by MRI that the mean renal growth was 2.7% at 6 months [19]. In our study, the measurement of renal volume by ultrasonography underestimates the real volume with a median error exceeding the expected annual variation in renal volume. Another CRISP study [16] demonstrated that the variability of the ultrasonography renal volumes calculated at an interval of one year in patients monitored for ADPKD was much higher than the volumes measured by MRI, suggesting a measurement error induced by the different operators. This did not favour the recommendation of the ultrasonography measurement as a method of close monitoring.

Nevertheless, ultrasonography may help detect a variation in the renal volume if the monitoring is carried out in a 2-year interval, since the renal growth is then about 10%. Moreover, the ultrasonography error may be negligible in certain situations where the monitoring of the renal growth may be less precise, in particular in the case of the monitoring of compensated renal hypertrophy with contralateral nephrectomy. For this reason, ultrasonography is more accessible and faster, and remains a good indication when compared with the CT-scan (no irradiation) or the MRI (claustrophobia, pacemaker...).

The concordance between the reference volume and the surface measurements was good although the precision was not sufficient to detect the annual increase in renal volume, including in the selected population of early PKAD patients.

The sonography error may be attributed to measurement errors or the use of the ellipsoid formula since the kidney is not a perfect ellipsoid. The low concordance between the ultrasonography widths and the CT-scan widths indicates the possibility of a measurement error: this predominated over the estimate of the thickness and the transverse width, data also found in the literature [14]. The deviation between the volumes of normal kidneys calculated by CT-scan or MRI and those measured directly using volumetry software has been shown to range from 15 to 25% [17,18,20]: the error was attributed to the ellipsoid formula. However, our figures were better. In fact, the comparison between the volume calculated by CT-scan and the measured volume found high ICC with a mean deviation of 7%. This result raises the question of the benefits of the use of ultrasonography volumetry software since, although more precise, is also time-consuming.

The arrival of matrix electronic arrays to calculate the renal volume from volumetric acquisition may improve the precision of the measurement and restore the place of ultrasound measurements [18].

Conclusion

Ultrasoundography is an efficient method to estimate the renal volume (with a correlation coefficient calculated at 0.86), although the precision is insufficient to detect low variations in the annual renal volume on kidneys with a large increase in size, in particular for the monitoring of early ADPKD patients under treatment to limit the development of kidney failure. This imprecision seems to be mainly related to the error in the measurement of the thickness and transverse width of the kidney.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


