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RESEARCH

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Quantification of liver fat using non-invasive MRI-PDFF technique versus guided biopsy in potential liver donor

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Abstract

Introduction Significant hepatic steatosis affects the outcome of surgery when living donors are transplanted. The gold standard for diagnosing and evaluating hepatic steatosis is hepatic imaging-guided biopsy. Hepatic steatosis assessment using MR spectroscopy and the proton density fat fraction (MR-PDFF) method has produced positive findings.

Objectives Is to compare the pre-operative assessment of liver fat quantification using MRI-PDFF methods, a non-invasive method, with histopathology.

Subjects and methods A 42 potential donors were then operated surgically for liver transplantation, consequently, were available for the assessment of the efficiency and sensitivity of the radiological findings MRI-PDFF procedures and imaging-guided liver biopsy. This radiological workup of these donors was done through a period of 7 months.

Results In many liver transplantations centers, liver imaging-guided biopsy histopathological examination is the gold standard. The study examined the MR proton density fat fraction modality, a recently developed test for hepatic steatosis measurement. The findings indicate 86.8% sensitivity, 50% specificity, 94.2% PDV, 28.5% NPV, 83.3% accuracy, and 0.684 AUC. On analyzing the fat percent, we found that the recorded fat percent using liver imaging-guided biopsy ranges between 1 and 10% with a median of 3. On the other hand, the recorded fat percent using MRI ranged between 2 and 15% with a median of 5.

Conclusion The non-invasive magnetic resonance hepatic proton density fat fraction approach using IDEAL sequence is a reliable and accurate means of quantitatively evaluating hepatic steatosis with excellent sensitivity, specificity, and accuracy.

Keywords MRI, MRI-PDFF, Fatty liver infiltration, Biopsy

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Introduction

In a living-donor liver transplantation, a piece of a normal living person's liver is surgically removed then implanted into a patient whose liver is nonfunctioning normally. Within a few months of the operation, the donor's hepatic left lobe develops and regains its normal volume, size, and capacity. Also, the recipient's transplanted liver develops and returns normal liver function [1].

The gold standard for determining whether someone has non-alcoholic fatty liver is the liver imaging-guided biopsy. It is considered invasive choice, and there is a chance of discomfort, bleeding, infection, and even death. Additionally, there might be sample error and observer variability in liver biopsies [2].

Therefore, it would be preferable to use non-invasive techniques to diagnose NAFLD. The techniques for measuring hepatic fat have recently seen substantial advancements. For measuring hepatic fat, magnetic resonance spectroscopy is largely recognized as most precise non-invasive technique [3].

Although MR spectroscopy only normally samples a small part of the liver, it takes long time to execute and analyze and requires specialized radiologist. An MR-based method for assessing the proton density of the fat fraction was recently created. Because MRI can more reliably and rapidly estimate the quantity of fat in all liver locations and because postprocessing is simpler and quicker than with magnetic resonance, this technology is seen to be an alternative to MRS [4].

To ensure safety and regeneration of the remaining liver, living hepatic donors go through a rigorous evaluation. The results regarding the living-donor liver transplantation, for both donors and recipients, are significantly impacted by steatosis. The allografts with moderate and severe macrosteatosis are infrequently used in the liver transplantation due to an increased risk of biliary problems, non-function, and dysfunction. Such a high degree of steatosis in LDLT can hinder the regeneration of the remaining liver. The assessment of liver steatosis in living donors is essential as most of the living-donor liver transplant programs limit the living liver donation to between 10 and 20% steatosis to maximize donor safety [5].

Aim of work

Compare the recent non-invasive magnetic resonance imaging (MR) methods in cases of pre-operative liver fat estimation versus histopathology.

Patients and methods

Forty-two potential donors in all were eligible to take part in the trial; of these, 30 patients were males, and 12 were females. The liver transplantation unit at the National Hepatology and Tropical Medicine Institute (NHTMI) referred them to the radiology department for a pre-operative evaluation (Figs. 1, 2, 3, and 4).

A retrospective study approved by the National Hepatology and Tropical Medicine Institute (NHTMI) in Egypt. Informed consent was waived because this was a retrospective study.

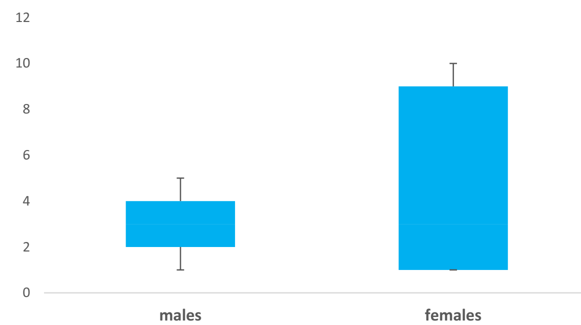


Fig. 1 The difference between the males and females regrading fat percent recorded through biopsy

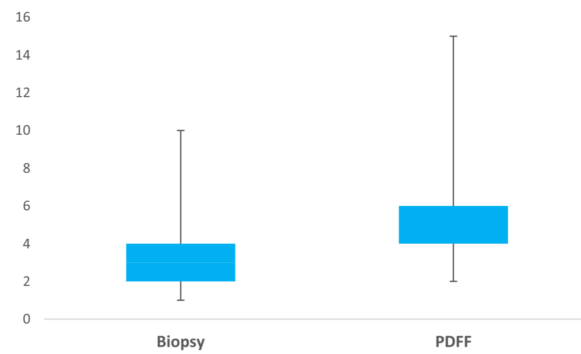


Fig. 2 The difference between the biopsy and PDFF regarding fat percentage

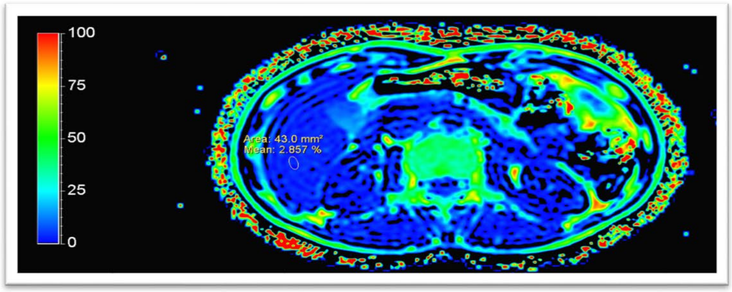
Inclusion criteria included adults above 18 years old. And below 45 years old, males and females

The 1st step assessment for donor preparation includes blood group and RH factor, HCV Ab, HBsAg, HBC Ag, SGOT, SGPT, alkaline phosphatase, GGT, album and total protein albumin, urea, creatinine, uric acid, Na, K, and Ca, CBC, PT, PC, PTT and INR, CRP, anti-bilharzial, lipid profile. Ultrasound abdomen and pelvis. Duplex for the portal vein, hepatic artery, and hepatic veins. MRCP, CT study triphasic for volumetry for potential donor. Liver biopsy sent to histopathology.

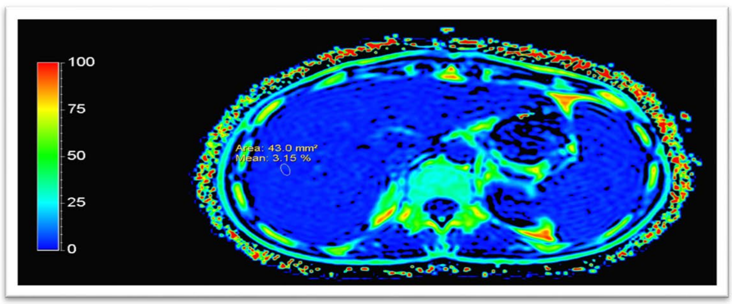
Exclusion criteria include younger than 18 years old and more than 45 years old, severe psychiatric disease, claustrophobia, BMI > 31, +ve HBsAg, and HCV Ab.

The selected donors were subjected to the full radiological survey of evaluation of hepatic steatosis using MRI-PDFF technique. Liver imaging-guided biopsy.

All 42 potential donors were then operated surgically for liver transplantation, consequently, were available for the assessment of the efficiency and sensitivity of the radiological findings MRI-PDFF procedures and liver biopsy. This radiological workup of these donors was done through a period of 7 months (Tables 1, 2, 3, and 4).



(A)



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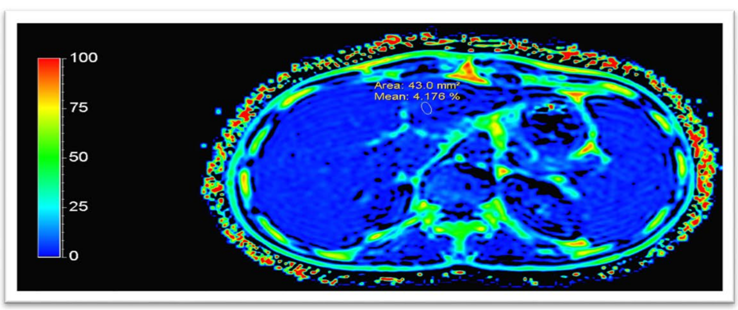
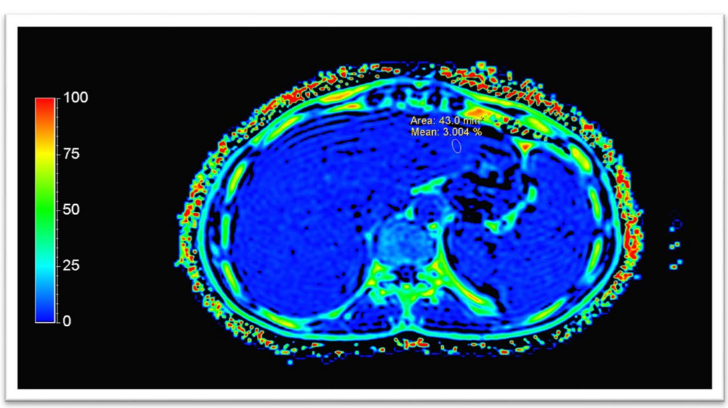
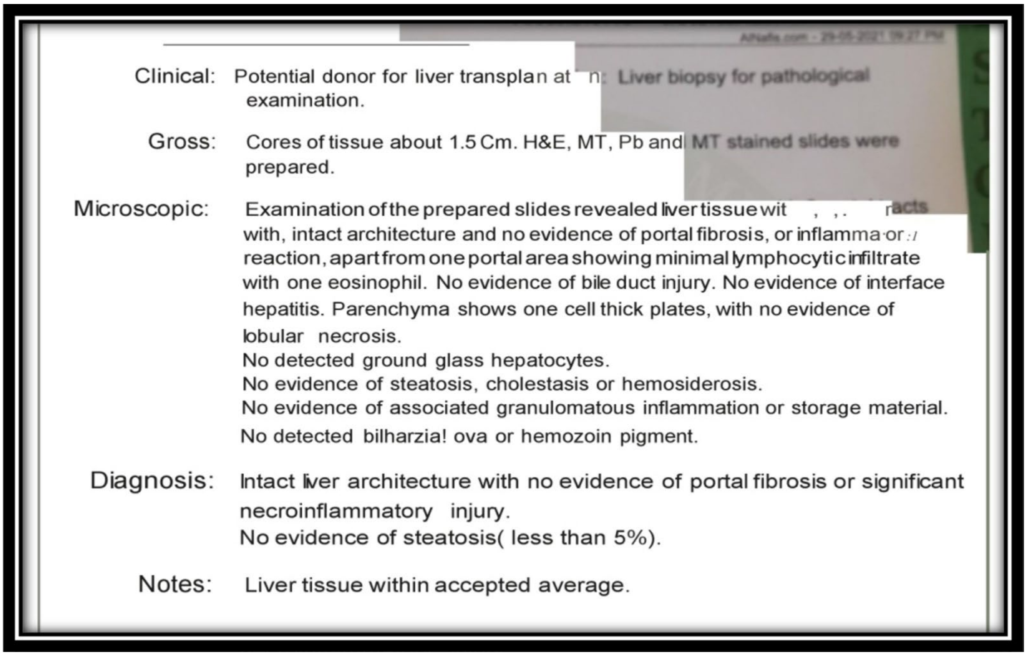


(C)



(D)

Fig. 3 Multiple MRI-PDFF liver sequences from (**a**) to (**d**) show a 28-year-old male with grade 0 steatosis (range: 2.9%–4.2%). For every subject, one segment obtained from the liver is displayed


Clinical: Potential donor for liver transplan at n: Liver biopsy for pathological examination.

Gross: Cores of tissue about 1.5 Cm. H&E, MT, Pb and MT stained slides were prepared.

Microscopic: Examination of the prepared slides revealed liver tissue wit , , . racts with, intact architecture and no evidence of portal fibrosis, or inflamma·or :/ reaction, apart from one portal area showing minimal lymphocytic infiltrate with one eosinophil. No evidence of bile duct injury. No evidence of interface hepatitis. Parenchyma shows one cell thick plates, with no evidence of lobular necrosis.
No detected ground glass hepatocytes.
No evidence of steatosis, cholestasis or hemosiderosis.
No evidence of associated granulomatous inflammation or storage material.
No detected bilharzia! ova or hemozoin pigment.

Diagnosis: Intact liver architecture with no evidence of portal fibrosis or significant necroinflammatory injury.
No evidence of steatosis(less than 5%).

Notes: Liver tissue within accepted average.

Fig. 4 Pathology report shows no fatty liver and the donor with steatosis less than 5%

Table 1 The difference between the males and females regrading fat percent recorded by biopsy

	Male	Female	*P* value
Fat percent	3 (2–4)	3 (1–9)	0.884
Mann–Whitney U-test			

Table 2 The median fat percent for selected patients ($n = 42$)

	Median (Q1–Q3)	Minimum	Maximum	Spearman correlation	*P* value
Biopsy	3 (2–4)	1	10	0.960*	< 0.001*
PDFF	5 (4–6)	2	15		

*Spearman correlation

Table 3 The agreement between the biopsy and PDFF in detection of the fat percentage among participants

MRI-PDFF	Biopsy		Total	*P*
	≤ 5%	> 5%		
≤ 5%	33 (86.8%)	2 (50%)	35 (83.3%)	0.060
> 5%	5 (13.2%)	2 (50%)	7 (16.7%)	
Total	38	4	42	

Table 4 The diagnostic accuracy of the PDFF in detection of fat percentage within participants

Statistic	Value	95% CI
AUC	0.684	0.523–0.819
Sensitivity	86.84%	71.91–95.59%
Specificity	50%	6.76–93.24%
Positive predictive value	94.29%	86.01–97.79%
Negative predictive value	28.57%	10.05–58.89%
Accuracy	83.33%	68.64–93.03%

MRI techniques for evaluation of hepatic steatosis

The liver signal is first divided into its fat and water components by the MRI methods used to assess hepatic steatosis, and the hepatic fat fraction is then determined.

The 42 living potential liver donors done MR imaging (MRI) at 1.5.0-T MR system (Philips Medical Systems) in the radiology department of the National Hepatology and tropical medicine research institute.

The donors were instructed to NPO (nil per os) for 4 h prior to MRI examination with early arrival 15–20 min for the subjects underwent breath-hold transverse T1 weighted in and opposed phase GE MRI and T2-weighted TSE MRI with fat saturation.

In order to acquire pictures using the original Dixon-based dual-echo approach, two TEs must be used: one at which the major fat peak (1.3 ppm) and the water peak

(4.7 ppm) are out of phase, and another at which the two peaks are in phase.

MRI-PDFF includes fat quantification, sequences include m Dixon–Quant (breath hold), water only, fat only, fat fraction, color overlay (blue for ped), every 20 intensity mean value = fat fraction

The 42 living potential liver donors done liver imaging-guided biopsy in the radiology department of the National Hepatology and tropical medicine research institute.

All images were reviewed by two experienced radiologists blindly.

Results

Upon examining the fat percentage, we discovered that it spans from 1 to 10%, with a median of 3 (2–4). Conversely, the fat percentage measured by MRI varied from 2 to 15%, with a median of 5 (4–6).

As the table below illustrates, we discovered that there was a substantial positive connection (Spearman correlation = 0.960, $p < 0.001$) between the two readings.

As indicated in the table below, we discovered that the MRI-PDFF true positive was 86.8% with a false-positive rate of 50% and the true negative was 50% with a false-negative rate of 13.2%.

As indicated in the table below, we discovered that MRI-PDFF is an effective method for determining the patient's percentage of body fat (AUC = 0.684, 95% CI 0.523–0.819) with 86.8% sensitivity, 50% specificity, and 83.3% accuracy.

Discussion

The main result of the study proves that MRI is a non-invasive substitute for liver imaging-guided biopsy to estimate hepatic fat and a helpful method for assessing living liver donors.

Both the donor and the receiver experience morbidity from liver steatosis in cases of the living-donor's liver transplantation. The evaluation of hepatic steatosis is crucial for choosing living liver donors since severe hepatic steatosis can affect the donor's postoperative results. Additionally, the recipient of steatosis graft in cases of liver transplantation experienced primary malfunction, early dysfunction, and poor graft survival as well as other problems [6].

Although numerous biochemical, anthropometric, and radiographic techniques have been thoroughly examined, liver-guided biopsy is currently the gold standard for the evaluation of degree of liver steatosis [7].

Ultrasonographic examination, CT, and MRI imaging are considered non-invasive imaging techniques that suggested to evaluate liver steatosis in living liver donors in order to get around these constraints. Unfortunately, these technologies are constrained by their high cost, low sensitivity, limited availability, and operator dependence. Furthermore, it is debatable whether non-invasive imaging techniques can accurately identify hepatic steatosis [8].

Studies have shown encouraging outcomes using MR spectroscopy and PDFF approach in assessing liver steatosis thanks to recent advancements in MR technology. Additionally, it has been demonstrated that MR elastography holds promise for hepatic fibrosis staging and NASH identification in NAFLD patients. Prior to liver transplantation, MR is commonly utilized as a non-invasive technique to assess the biliary and vascular anatomy of potential living liver donors without radiation-related biological risks [9].

Forty-two potential donors met the study's eligibility requirements. Of them, 31% were male, and 26.2% were female, representing 73.8% of participants and potential donors, respectively. Their average age, which varied from 20 to 42 years old, was discovered to be 28.52 ± 5.55 years old.

The study by Broering et al. [10] provided support for our findings since it mentioned that 150 possible living liver donors were taken into consideration for the analysis. The cohort's mean age was 30.0 ± 7.0 years, with 73.3% of the participants being male, resulting in a 3:1 male-to-female ratio.

Also, Kim et al. [11] demonstrated that of the 79 donors, 53 (67.1%) were men, and 26 (32.9%) were women. The median age was 32 years (range: 18–68 years).

The results of the current investigation revealed that, while analyzing their BMI, we discovered that the BMI ranged between 19 and 30 kg/m^2, with a mean of 25.21 3.64 kg/m^2. After reviewing the patients' heights, we discovered that their average height was 170.5 cm, with a range of 156–188 cm. Reviewing participant weights revealed that it spans from 53 to 88 kilograms, and the median value of 76 (67.75–80) kilograms.

Keeping with our findings, van Werven et al.'s study [12] found that the average body mass index was 27.1 kg/m^2 (range, 20.2–40.6 kg/m^2), with men's averages being 26.2 kg/m^2 (range, 20.8–34.0 kg/m^2) and women's averages being 28 kg/m^2 (range, 20.2–40.6 kg/m^2). About 41% (19 of 46) of the patients had a normal weight, and 59% (27 of 46) were overweight, with a normal body mass between 20 and 25 kg/m^2.

Similarly, Qi et al. [13] revealed that the mean BMI of their studied group was 27 ± 4 kg/m^2, their mean height was 169 ± 10 cm, and their mean weight was 77 ± 15 kg.

Additionally, BMI used as a stand-in for the presence of steatosis. The odds ratio for NAFLD was 21.8 for BMI between 23 and 25 kg/m^2, but 29.9 for BMI 25 kg/m^2 in a study of 250 patients with NAFLD compared to the control group Zheng et al. [14]. Patients with a BMI under 23 kg/m^2 did not experience a higher odds ratio. Additionally, among patients with NAFLD, obesity was linked to an increased risk of liver fibrosis Lu et al. [15].

According to the current study, the recorded fat percent has a median of 3 (2–3) and ranges from 2 to 5%. Conversely, the fat percentage measured by MRI varied from 2 to 8%, with a median of 4 [4, 5]. We discovered a substantial positive connection (Spearman correlation = 0.802, $p < 0.001$) between the two readings.

Comparatively, according to Qi et al. [13], of the 184 living hepatic donors who underwent MRI-PDFF, 149 (81%) had no steatosis, 31 (17%) had mild steatosis, and 4 (2%) had substantial steatosis. In 133 donors with a numerical steatosis %, there were no disparities between the values given in the original MRI reports and the MRI-PDFF estimated by study radiologists. Thirty-three (18%) prospective donors chose not to donate, 7 (4%) made a donation to a child recipient, and 1 (0.5%) was still awaiting donation surgery at the time of this analysis. The final analysis contained 143 (78%) donors and their matching beneficiaries. Three potential donors were turned down because of moderate-to-severe steatosis, with a fat fraction of 20.5%, 23.7%, and 39.7% in donors compared to the non-donors (3.8% [2.5–8.6]; $p = 0.07$). Among the real donors, 121 (84%) had no steatosis, 21 (15%) had mild steatosis, and 1 (1%) had significant steatosis. The donor had a modest case of steatosis with a fat fraction of 20.3%.

In contrast, none of the patients in the Kim et al. [11] study got their liver biopsy for screening purpose during the pretransplant. On frozen section or histology, none of the 79 donors had macro- or microsteatosis greater than 30%. The range of macrosteatosis and microsteatosis was 0%–15%, with 1% as the median. Hepatic steatosis affected the liver on average to a median extent of 2% (0–25%). There were 3 (3.8%), 4 (5.1%), and 8 (10.1%) individuals, respectively, with macro- and microsteatosis or total hepatic steatosis higher than 10%. Accordingly, hepatectomy was performed on all living liver donors.

Twenty-three patients in the study by van Werven et al. [12] had no macrovesicular steatosis (0–5%), 11 had mild (5–33%), 9 moderate (33–66%), and 3 severe (> 66%). Stronger correlations between histopathologic steatosis evaluation and the MR imaging and 1H MR spectroscopic measurements of the hepatic fat were found to be $r = 0.85$, $P = 0.001$ and $r = 0.86$, $P = 0.001$, respectively.

The mean PDFF determined by MR imaging was 18.1% 9.5 (standard deviation), according to Idilman et al. [16]. A strong association ($r = 0.82$) between the PDFF and liver biopsy was found for the measurement of hepatic steatosis. With an area under the curve of 0.95, PDFF was successful in separating moderate/severe hepatic steatosis from mild or non-hepatic steatosis. When fibrosis was present, the association between the biopsy and the PDFF-determined steatosis was less apparent than when it was not ($r = 0.60$ vs. 0.86; $P = 0.02$).

Conclusion

The study proves that MRI is a non-invasive substitute for liver-guided biopsy to estimate hepatic fat and a helpful method for assessing living liver donors, in order to sum up. We demonstrate that the non-invasive MR hepatic PDFF technique with the IDEAL sequence is accurate, dependable method with excellent sensitivity of about 85.7%, specificity 97.5%, and the accuracy 95.7% for quantifying hepatic steatosis. Pre-operative liver examination in living donors is advised, as is selective hepatic biopsy in donor candidates who found significant hepatic steatosis on MR-PDFF findings.

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Author contributions
All authors have read and approved the manuscript. Hany el-assaly (HE), Laila abd el-moaty (LA), Reda Saad (RS), and Mohamed Mohsen (MM) and Ayman osama (AO) contributed equally to this work. HE and RS designed research. HE and LA performed research. HA and LA analyzed data. HE, MM, and AO wrote the paper.

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Availability of data and materials
All the datasets used and analyzed during this study are available with the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study way approved by the research ethics committee of the radiology department of the Faculty of medicine Cairo University on 1/8/2021, reference number of approval: REC 1-8-2021. All patients included in this study gave a written informed consent to participate in the research. If the patient was less than 16 years old, or unconscious at the time of study, written informed consent was given by their parent or legal guardian.

Consent for publication
All patients included in this study gave a written informed consent to publish the data contained in this study. If the patient was less than 16 years old, or unconscious at the time of study, written informed consent was given by their parent or legal guardian.

Competing interests
The authors declare that they have no competing interests.

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