

**PEDRO IVO C. RAVIZZINI**

**ANÁLISE COMPARATIVA DA TAXA DE SUCESSO E COMPLICAÇÕES  
EM BIÓPSIAS ORIENTADAS POR ULTRASSONOGRAFIA DE RINS  
NATIVOS EM DECÚBITO SUPINO ANTEROLATERAL COM FLANCO  
LIVRE NA POPULAÇÃO PEDIÁTRICA E ADULTA**

**TESE APRESENTADA AO PROGRAMA DE PÓS-  
GRADUAÇÃO DA FACULDADE DE CIÊNCIAS  
MÉDICAS DA SANTA CASA DE SÃO PAULO PARA  
OBTENÇÃO DO TÍTULO DE DOUTOR EM CIÊNCIAS  
DA SAÚDE**

**SÃO PAULO  
2025**

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**Orientador: Prof. Dr. LUIS GUSTAVO MORATO DE TOLEDO  
Coorientador: Prof. Dr. EDUARDO DE FARIA CASTRO FLEURY**

**SÃO PAULO  
2025**

## **FICHA CATALOGRÁFICA**

**Preparada pela Biblioteca Central da  
Faculdade de Ciências Médicas da Santa Casa de São Paulo**

Ravizzini, Pedro Ivo C.

Análise comparativa da taxa de sucesso e complicações em biópsias orientadas por ultrassonografia de rins nativos em decúbito supino anterolateral com flanco livre na população pediátrica e adulta./ Pedro Ivo C. Ravizzini. São Paulo, 2025.

Tese de Doutorado. Faculdade de Ciências Médicas da Santa Casa de São Paulo – Curso de Pós-Graduação em Ciências da Saúde.

Área de Concentração: Ciências da Saúde

Orientador: Luis Gustavo Morato de Toledo

Coorientador: Eduardo de Faria Castro Fleury

1. Rim 2. Nefropatias/ diagnóstico por imagem 3.  
Ultrassonografia de intervenção 4. Biópsia guiada por imagem

BC-FCMSCSP/40-25

## *Dedicatória*

**Aos que dão sentido à minha vida:  
minha mãe, Melba, por seu amor e força;  
meu pai, Pedro Ivo, cuja memória nos inspira e guia;  
minha esposa, Christiane, meu porto seguro;  
meu irmão, Gregory, laço Inabalável; Gianni e Sophie, nossa renovação.**

*"Amigos são as testemunhas silenciosas de nossa história. Eles celebram nossas vitórias, compartilham nossas dores e, sem precisar de palavras, nos mostram que nunca estamos verdadeiramente sós."*  
**Aristóteles (inspirado em "Ética a Nicômaco")**

*"Medicina não é apenas uma profissão; é um chamado para aliviar o sofrimento alheio. O verdadeiro médico não vê doenças, mas pessoas que precisam de cuidado, dignidade e esperança."*  
**William Osler (pai da medicina moderna)**

*"Ser médico é abraçar a responsabilidade de ser eterno aprendiz. Cada paciente é um mestre, cada caso um novo capítulo no livro infinito da ciência e da compaixão."*  
**Hipócrates (inspirado no Juramento Hipocrático)**

*"Ajudar o próximo não é um ato de grandeza, mas de humanidade. Nas pequenas ações — um olhar, um gesto, um silêncio compartilhado — reside o verdadeiro significado da existência."*  
**Albert Schweitzer (médico e Nobel da Paz)**

## ***Agradecimentos***

À Irmandade da Santa Casa de Misericórdia de São Paulo, em especial ao provedor Dr. Vicente Renato Paolillo, pelo inestimável apoio institucional que tornou esta pesquisa possível.

À Faculdade de Ciências Médicas da Santa Casa de São Paulo e ao diretor Prof. Dr. Carlos Alberto Herrerias de Campos, pelo compromisso com a excelência acadêmica que tanto inspirou meu percurso científico.

Ao meu orientador, Prof. Dr. Luis Gustavo Morato de Toledo, pela orientação sábia, pelo constante estímulo à superação e por me mostrar que a ciência se faz com rigor e paixão.

Ao meu coorientador Prof. Dr. Eduardo de Faria Castro Fleury, cuja amizade, competência e generosidade foram fundamentais em cada etapa deste trabalho.

Aos colegas do Serviço de Urologia, liderados pelo Dr. Roni de Carvalho Fernandes, pelas valiosas oportunidades de aprendizado e pelo exemplo diário de dedicação aos pacientes.

Aos profissionais do Serviço de Radiologia e Diagnóstico por Imagem, em especial à equipe de Radiologia Intervencionista Percutânea, pelo compartilhamento de conhecimentos e pela parceria nos momentos mais desafiadores.

À minha mãe, Melba, pelo amor incondicional e por ser o alicerce que me permitiu chegar até aqui.

Ao meu pai, Pedro Ivo, médico inspirador e meu maior exemplo de vida, cujo legado orienta minha jornada profissional e pessoal. Esta conquista é, em grande medida, fruto dos valores que você me ensinou.

## ***Abreviaturas e símbolos***

USPB - Ultrasound-guided percutaneous biopsy

SALP - Supine Oblique Antero-lateral Position

FF-SALP - Free-Flank Supine Oblique Antero-lateral Position

PP - Prone Position

G - Gauge

y/o - Years old

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## 1. INTRODUÇÃO

As doenças renais representam um desafio global de saúde pública com impacto crescente na morbimortalidade e nos sistemas de saúde. Dados da Sociedade Internacional de Nefrologia revelam que aproximadamente 850 milhões de pessoas são afetadas por doenças renais em todo o mundo, sendo a doença renal crônica responsável por pelo menos 2,4 milhões de mortes anuais, configurando-se como a sexta causa de óbito de crescimento mais acelerado globalmente <sup>(1)</sup>. Nos países em desenvolvimento, esse cenário é particularmente preocupante, com taxas de incidência de doença renal crônica avançada aumentando cerca de 8% ao ano, impulsionadas pelo envelhecimento populacional e pela epidemia de doenças metabólicas <sup>(2)</sup>.

Dentre as diversas condições renais, as glomerulopatias primárias e secundárias merecem destaque especial, sendo responsáveis por aproximadamente 20-30% dos casos de insuficiência renal terminal <sup>(3)</sup>. A glomeruloesclerose segmentar e focal representa 15-20% das biópsias renais em adultos e 7-20% em crianças, enquanto a nefropatia por IgA afeta predominantemente adolescentes e adultos jovens, com prevalência variando de 10-45% conforme a região geográfica <sup>(4)</sup>. As vasculites associadas a ANCA apresentam incidência anual de 13-20 casos por milhão na população adulta, frequentemente exigindo confirmação histológica para orientação terapêutica adequada <sup>(5)</sup>.

No contexto brasileiro, os dados do Censo Brasileiro de Nefrologia demonstram que as glomerulonefrites primárias constituem a terceira causa de entrada em diálise, correspondendo a 12,8% dos casos <sup>(6)</sup>. Estudo multicêntrico nacional envolvendo 9.528 biópsias renais identificou que as principais indicações em adultos foram síndrome nefrótica (31,3%), insuficiência renal aguda (24,1%) e hematúria/proteinúria assintomática (18,7%), enquanto na população pediátrica predominou a síndrome nefrótica (58,4%) <sup>(7)</sup>. A análise histopatológica evidenciou diferenças marcantes entre faixas etárias, com lesões mínimas correspondendo a 22,3% dos diagnósticos em crianças, contra apenas 6,5% em adultos <sup>(8)</sup>.

A importância da biópsia renal no cenário nacional torna-se evidente quando se considera que em 30-40% dos casos o diagnóstico histopatológico resulta em modificações significativas na conduta terapêutica, particularmente em pacientes com suspeita de nefrite lúpica, vasculites ou doenças de depósito <sup>(9)</sup>. No contexto pediátrico, esse procedimento assume papel ainda mais crucial, visto que o tratamento da síndrome nefrótica esteroidorresistente - que afeta 10-20% das

crianças com síndrome nefrótica - é totalmente guiado pelo padrão histológico identificado <sup>(10)</sup>.

A biópsia renal percutânea guiada por ultrassonografia, introduzida por Iversen e Brun em 1951 <sup>(11)</sup>, revolucionou o diagnóstico das doenças glomerulares, tornando-se procedimento indispensável na prática nefrológica contemporânea. Estudos comparativos demonstram que essa abordagem apresenta taxas de sucesso que variam de 93-97% na obtenção de tecido renal adequado, com complicações maiores ocorrendo em apenas 0-1,6% dos casos <sup>(12)</sup>.

A técnica convencional realizada em posição prona permanece como abordagem mais utilizada mundialmente para biópsias guiadas por ultrassonografia de rins nativos <sup>(13)</sup>. Essa posição oferece vantagens anatômicas importantes, incluindo menor distância entre a pele e o parênquima renal (3-5 cm em adultos) e trajetória que evita estruturas vasculares significativas <sup>(14)</sup>. Entretanto, revisões sistemáticas recentes destacam limitações importantes da posição prona em subgrupos específicos de pacientes <sup>(15)</sup>.

Pacientes obesos (IMC >30 kg/m<sup>2</sup>) apresentam maior espessura do tecido adiposo subcutâneo, o que pode aumentar a distância pele-rim em até 300%, elevando o risco de obtenção de amostras inadequadas <sup>(16)</sup>. Nos idosos (>65 anos), a diminuição da massa renal cortical (20-25% menos glomérulos viáveis) associada à maior fragilidade vascular amplia significativamente os riscos hemorrágicos <sup>(17)</sup>. Indivíduos com comprometimento respiratório frequentemente desenvolvem dessaturações significativas (SpO<sub>2</sub> <90% em 18% dos casos) devido à restrição ventilatória na posição prona <sup>(18)</sup>. Já em crianças com a necessidade de anestesia geral o decúbito prono pode tornar o procedimento particularmente desafiador <sup>(19)</sup>.

Diante dessas limitações, a biópsia de rins nativos guiada por ultrassonografia em posição supino ântero-lateral emergiu como abordagem alternativa com vantagens teóricas relevantes. Descrita inicialmente por Enríquez et al. em 2003 para pacientes obesos <sup>(20)</sup>, essa técnica foi subsequentemente adaptada para outras populações com contra-indicações à posição prona <sup>(21)</sup>. Entre seus principais benefícios destacam-se o melhor controle das vias aéreas durante anestesia geral (especialmente relevante em pediatria) <sup>(22)</sup>, redução de 40-60% na incidência de complicações respiratórias perioperatórias quando comparada à posição prona <sup>(23)</sup>, acesso facilitado ao rim direito (5-8 cm mais caudal que o esquerdo) <sup>(24)</sup>, e maior conforto para pacientes idosos ou com limitações musculoesqueléticas <sup>(25)</sup>.

Estudo prospectivo randomizado realizado por Gesualdo et al. (2008) comparando posição prona versus supino ântero-lateral em 312 pacientes adultos demonstrou equivalência no rendimento glomerular ( $16,7 \pm 9,3$  vs.  $15,9 \pm 8,7$  glomérulos;  $p=0,42$ ) e taxas de complicações ( $9,6\%$  vs  $7,1\%$ ;  $p=0,38$ ) <sup>(26)</sup>.

Esta linha pesquisa surge no contexto de importantes lacunas no conhecimento científico atual, incluindo a carência de estudos comparativos robustos entre populações pediátrica e adulta submetidas à técnica supino ântero-lateral, a necessidade de avaliação sistemática do rendimento glomerular por faixa etária, a falta de padronização técnica para grupos especiais (obesos, idosos, crianças) e a insuficiência de dados sobre complicações a longo prazo (>30 dias) <sup>(27-30)</sup>.

Nesse cenário, nossa pesquisa procurou comparar a taxa de sucesso (rendimento glomerular) e as complicações das biópsias renais percutâneas guiadas por ultrassonografia em decúbito supino anterolateral com flanco livre entre populações pediátrica e adulta, avaliando a segurança, eficácia e vantagens técnicas dessa abordagem inovadora.

A relevância campo de investigação deve transcender o aspecto técnico, podendo impactar diretamente a prática clínica ao estabelecer protocolos baseados em evidências para diferentes faixas etárias, reduzir a necessidade de procedimentos repetidos em populações vulneráveis, otimizar o uso de recursos em serviços de nefrologia intervencionista e melhorar a experiência do paciente durante esse procedimento diagnóstico essencial <sup>(31-34)</sup>.

Os resultados obtidos poderão subsidiar a elaboração de diretrizes clínicas nacionais e internacionais, particularmente no manejo de pacientes pediátricos e adultos com contraindicações à posição prona tradicional <sup>(35)</sup>. Adicionalmente, a análise estratificada por subgrupos etários na população adulta (>18-40, >40-60, >60 anos) fornecerá insights valiosos sobre as variações anatômico-fisiológicas que influenciam os resultados do procedimento <sup>(36)</sup>.

## **2. OBJETIVOS**

**Objetivos desta Linha de Pesquisa foram:**

### **Objetivo Geral**

Comparar a taxa de sucesso (rendimento glomerular) e as complicações das biópsias renais percutâneas guiadas por ultrassonografia em decúbito supino anterolateral com flanco livre (FF-SALP) entre populações pediátrica e adulta, avaliando a segurança, eficácia e vantagens técnicas dessa abordagem.

### **Objetivos Específicos**

1. Avaliar a segurança da técnica FF-SALP:

- Comparar as taxas de complicações (maiores e menores) entre pacientes pediátricos e adultos.

2. Analisar o rendimento diagnóstico:

- Quantificar o número médio de glomérulos obtidos por amostra em cada grupo etário.

- Determinar a proporção de amostras com  $\geq 10$  glomérulos (critério de adequação histopatológica).

3. Comparar subgrupos adultos:

- Estratificar adultos em faixas etárias (>18–40 anos, >40–60 anos, >60 anos) para avaliar diferenças no rendimento glomerular e complicações.

4. Otimizar o procedimento para populações específicas:

- Investigar as vantagens da FF-SALP em crianças (ex.: manejo anestésico, conforto) e em adultos com contraindicações para a posição prona (obesos, idosos, pacientes com comprometimento respiratório)

5. Contribuir para diretrizes clínicas:

- Propor recomendações baseadas em evidências para a escolha da posição e técnica de biópsia renal conforme características do paciente.

**Justificativa dos Objetivos**

1. Lacuna no conhecimento: Apesar da ampla utilização da posição prona, há poucos estudos sobre a FF-SALP, especialmente em crianças.
2. Vantagens potenciais: Melhor acesso às vias aéreas, redução de riscos anestésicos em pediatria e adaptação para pacientes com limitações anatômicas.
3. Impacto clínico: Os resultados podem padronizar uma técnica mais segura e acessível, beneficiando os pacientes dos serviços de nefrologia e radiologia intervencionista.

### **3. METODOLOGIA**

#### **Desenho do Estudo**

Este trabalho constitui uma coorte retrospectiva com coleta prospectiva de dados, realizada no Setor de Radiologia Intervencionista do Serviço de Radiologia e Diagnóstico por Imagem da Santa Casa de Misericórdia de São Paulo. O período de estudo compreendeu treze anos, entre fevereiro de 2008 e fevereiro de 2021, permitindo a inclusão de um número significativo de procedimentos para análise comparativa robusta entre as diferentes faixas etárias.

#### **População**

Os critérios de inclusão foram delineados para abranger pacientes submetidos à biópsia renal percutânea guiada por ultrassom de rins nativos, com idades variando entre 0,5 e 85 anos. Todos os procedimentos incluídos foram realizados na posição supina ântero-lateral com flanco livre, utilizando protocolo técnico padronizado. Foram excluídos da análise os casos de biópsias de aloenxertos renais e de massas renais, visando manter a homogeneidade da amostra em relação ao tecido analisado.

A amostra final compreendeu 431 procedimentos, estratificados em dois grupos principais: 215 pacientes pediátricos ( $\leq 18$  anos) e 216 pacientes adultos ( $> 18$  anos). Esta divisão permitiu comparações diretas entre as populações, além de análises subsequentes por subgrupos etários na população adulta.

#### **Variáveis Estudadas**

As variáveis primárias de interesse incluíram o número de glomérulos por amostra e as taxas de complicações, categorizadas como maiores ou menores conforme critérios estabelecidos na literatura. Como variáveis secundárias, foram analisados o número de fragmentos obtidos, a adequação histopatológica (definida como presença de  $\geq 10$  glomérulos por amostra) e a distribuição dos diagnósticos histopatológicos por faixa etária.

#### **Procedimentos**

O preparo dos pacientes seguiu protocolo institucional padronizado, incluindo jejum de 8 horas para os submetidos à anestesia geral e 4 horas para aqueles sob anestesia local. Todos os pacientes foram submetidos à avaliação laboratorial prévia, com ênfase na contagem plaquetária ( $> 50.000/\text{mm}^3$ ) e no índice internacional normalizado (INR  $\leq 1,5$ ), garantindo condições adequadas de hemostasia para o procedimento.

A técnica de biópsia empregada consistiu no posicionamento em decúbito dorsal modificado, com elevação de cerca de  $30^\circ$  a  $40^\circ$  do flanco ipsilateral ao rim

a ser biopsiado. Esta abordagem, denominada posição supina ântero-lateral com flanco livre, permite acesso adequado ao rim enquanto mantém as vias aéreas acessíveis para o anestesiológico. A visualização ultrassonográfica foi realizada com transdutor convexo de 5MHz, proporcionando imagens de alta qualidade para planejamento da trajetória da agulha.

Os fragmentos foram obtidos utilizando agulha semiautomática 18G (modelo SuperCore II - Argon Medical, Frisco, Texas), com pelo menos duas amostras colhidas do terço médio do rim, região que apresenta maior comprimento transversal do córtex renal e, conseqüentemente, maior probabilidade de conter material suficiente para análise. O pós-operatório imediato incluiu ultrassom de controle após 2 horas e avaliação sistemática para detecção de hematúria macroscópica.

## **Análise Estatística**

A análise dos dados foi conduzida utilizando métodos estatísticos apropriados para cada tipo de variável. Para as variáveis contínuas, foram empregados testes ANOVA com testes *post-hoc* de Tukey ou teste de Mann-Whitney, conforme a distribuição dos dados. As variáveis categóricas foram analisadas através do teste Qui-quadrado ou teste exato de Fisher quando aplicável. Adotou-se nível de significância de  $p < 0,05$  para todas as análises, que foram realizadas utilizando o software SPSS versão 25.0 (IBM Corp. Released 2017. IBM SPSS. Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Um valor de  $p < 0,05$  foi considerado estatisticamente significativo.

## **4. RESULTADOS**

**4.1. Artigo 1: O artigo a seguir foi publicado na revista Abdominal Radiology**



# Comparative analysis of ultrasound-guided percutaneous biopsy of native kidneys in children and adults using the free-flank supine antero-lateral decubitus positioning

Pedro Ivo C. Ravizzini<sup>1,2</sup> · Henrique Lino<sup>1</sup> · Eduardo de Faria Castro Fleury<sup>1</sup> · Daniel Azevedo Rangel<sup>1</sup> · Luís Gustavo Morato de Toledo<sup>2</sup>

Received: 27 December 2023 / Revised: 22 March 2024 / Accepted: 23 March 2024  
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## Abstract

**Purpose** Ultrasound-guided percutaneous biopsy (USPB) of the native kidneys is the preferred diagnostic method for several nephrological conditions in both adult and pediatric populations. Conventionally, native kidney biopsies are conducted with patients in the prone position (PP). However, an alternative approach involving the supine oblique antero-lateral position (SALP) has been explored, particularly for individuals who are obese, elderly, or critically ill.

**Methods** This study aimed to assess the feasibility and outcomes of USPB performed in SALP with a Free-Flank setting (FF-SALP) in pediatric patients (Group A) compared to adults (Group B). Data from kidney biopsies conducted between 2008 and 2021 were gathered. The study focused on the safety and the prevalence of biopsy samples containing a minimum of 10 glomeruli, histopathological yield in both groups.

**Results** Complication rates were low in both groups (5.6% vs. 3.7%;  $p = 0.454$ ), without major complications noted. The pediatric group achieved a significantly higher mean number of glomeruli per biopsy compared to the adult group ( $20.6 \pm 12.3$  vs.  $15.7 \pm 9.4$ ;  $p < 0.001$ ). However, when evaluating the minimum threshold of 10 glomeruli (76.3% vs. 68.5%;  $p = 0.072$ ) and histopathologic yield (95.3% vs. 93.5%;  $p = 0.408$ ), no differences were observed between groups.

**Conclusion** USPB of native kidneys in the FF-SALP position is a safe and effective method for tissue sampling in patients with parenchymal disease. It demonstrated comparable diagnostic yields and complication rates in the pediatric and adult populations, providing advantages in terms of airway management, making it particularly useful for pediatric patients that require general anesthesia.

**Keywords** Kidney · Renal · Biopsy · Ultrasound · Percutaneous · Anesthesia

## Abbreviations

|         |                                                   |
|---------|---------------------------------------------------|
| USPB    | Ultrasound-guided percutaneous biopsy             |
| SALP    | Supine Oblique Antero-lateral Position            |
| FF-SALP | Free-Flank Supine Oblique Antero-lateral Position |
| PP      | Prone Position                                    |
| G       | Gauge                                             |
| y/o     | Years old                                         |

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## Introduction

Native kidney biopsy is essential for establishing diagnosis, prognosis, and guiding treatment for different nephrological disorders [1–4]. Ultrasound-guided percutaneous biopsy (USPB) is considered the gold standard due to its safety and low complication rates, providing adequate renal tissue sampling for histopathological study, both in adults and in the pediatric population [5–11].

The standard positioning for ultrasound-guided renal biopsy is the prone position (PP), with access through the posterior abdominal wall, since the kidneys are closer to the skin in this topography [5, 8, 9].

The technique of ultrasound-guided renal biopsy in the supine oblique antero-lateral position (SALP) has also been described in adults, posing as an alternative for obese patients, the elderly, those with respiratory restriction, or

under mechanical ventilation [12, 13]. This position also allows better access and control of the airways, avoids pressure of the anterior thoracic and abdominal walls, and facilitates the control of any hemodynamic and ventilatory complications during the biopsy. However, to our knowledge, the application of this technique in pediatric patients has never been reported. Moreover, adding a space between the cushions to elevate the patient to the SALP leaves the ipsilateral flank totally free for a wide range of biopsy needle skin insertion points, which is a novel technical adjunct that could facilitate the procedure.

The present study aims at evaluating safety, effectiveness, and possible advantages of ultrasound-guided percutaneous biopsy in SALP, with the addition of a Free-Flank setting (FF-SALP), for native kidneys in the pediatric population, and compare it to the adult patients undergoing biopsies with the same approach.

## Materials and methods

Retrospective cohort study with prospective data collection in the Interventional Radiology Service of the Department of Radiology—Santa Casa de Misericórdia de São Paulo—Brazil. Data were obtained from native kidney biopsies performed from February 2008 to February 2021, including pediatric (up to 18 y/o) and adult (older than 18 y/o) patients, allocated in two separate groups. Patients submitted to kidney allograft biopsy or renal neoplasms biopsy were excluded from the analysis. The study was approved by the Institutional Review Board of the Santa Casa de São Paulo.

Main objective: analysis of the safety and complications of ultrasound native kidney biopsies in the FF-SALP, comparing the pediatric and adult groups. Safety of the procedure was evaluated by documenting unexpected events, complications, and the need for urgent medical support measures during biopsy.

Complications were categorized as major or minor, as classified by Gesualdo et al. [9] and Visconti et al. [2]. Macroscopic hematuria, perinephric/subcapsular renal hematoma (< 5.0 ml), were classified as minor complications since they generally resolved spontaneously without the need for additional intervention. Acute renal bleeding with hypotension or hemodynamic instability, acute renal obstruction, septicemia, pseudoaneurysm, arteriovenous fistula, and other conditions requiring surgical intervention, transfusions or death were classified as major complications.

## Secondary objective

Analysis of the effectiveness using the mean total number of glomeruli per case in the biopsy samples and the prevalence of conclusive histopathological results per case, comparing

the pediatric and adult groups. Kidney biopsies were considered optimal when cortical fragments resulted in at least 10 or more glomeruli for histopathological analysis. Despite the number of glomeruli obtained by case, the proportion of conclusive histopathological results was also compared between the two groups.

## Patient preparation

Patients were tested to have at least 50.000 platelets, INR (international normalized ratio) up to 1.5 and Hemoglobin of at least 8 g/dL. A pre-procedure urinalysis sample was taken. Anticoagulant medications were suspended accordingly. An 8 h fasting was oriented before general anesthesia and 4 h, for local anesthesia. When needed, general anesthesia was performed using a laryngeal mask for mechanical ventilation.

Biopsy technique: Kidney biopsies were performed under the supervision by the same interventional radiology assistant and a 4th year designated interventional radiology resident of our interventional radiology residency program. Right kidneys were preferred due to their lower and more favorable anatomical position, but when atrophic, absent, or less accessible, a kidney biopsy of the left unit was executed in the same fashion.

Patients were positioned by placing separate cushions under the thoracic and gluteal region, elevating the ipsilateral flank of the renal unit to be biopsied. A space between the cushions was left free exposing the ipsilateral flank for easy access of the biopsy needle. A flank elevation around 30° to 40° was used. The homolateral arm was left resting on the chest, and the legs were slightly flexed, accommodated, and protected with cushions for patient comfort (Fig. 1).

Renal sonography was performed with either an Envisor C HD or Affiniti 70 devices (Philips Ultrasound, Inc. Bothell, Washington, United States), using 5 MHz convex



**Fig. 1** Free-Flank Supine antero-lateral position with elevation of around 30° to 40°. Patient under general anesthesia with a laryngeal mask

transducers. Kidney measurements were taken, and sonographic programming was performed for possible interpositions of organs and structures in the planned trajectory for the biopsy needle. Asepsis and antisepsis measures were carried out. Local anesthesia was administered to the skin, subcutaneous tissue, and muscle planes with 1% lidocaine hydrochloride under ultrasound guidance. Finally, a puncture orifice was made in the skin with a  $1.2 \times 40$  mm hypodermic needle and a disposable semi-automatic 18G needle (Super core II—Argon Medical, Frisco, Texas) was advanced towards the renal capsule under ultrasound guidance with the free-hand technique (i.e., without the aid of an ultrasound needle guiding device) (Fig. 2). Core biopsies of the renal cortex were obtained either on the anterior or the posterior aspect of the kidney, as most favorable for each case, guided by a transverse image of the renal unit. Biopsies were performed at the middle third of the kidney, aiming at the deep cortical layer in the transverse axis of the renal unit. At least two biopsy cores were obtained in each case with the needle specimen notch setting adjusted to 20 mm. Fragments were macroscopically evaluated on site for a minimum size of at least 1 cm each.

A sonographic control study was performed in all patients after 2 h of observation. Vital signs were measured, and a urine sample was taken for visual evaluation for macroscopic hematuria. When macroscopic hematuria or perirenal fluid was evident, the patient received additional prophylaxis with 50 mg/kg of cefazolin for 7 days, as well as symptomatic medication as needed.



**Fig. 2** Sonographic biopsy technique for the right kidney and scan showing sampling from the ventral aspect of middle third of the kidney

**Statistical Analysis:** In the descriptive analysis, for quantitative variables, mean, standard deviation, and range are presented (minimum–maximum), while for qualitative variables, frequency and percentage are provided. For comparing groups, when the response variable is quantitative, ANOVA was used. In the presence of variance heterogeneity between groups, the Mann–Whitney test is employed. When the response variable is qualitative, the Chi-square test or Fisher's Exact test was used. The significance level considered was 5%. All calculations were carried out using SPSS Statistics software, version 25.0 (SPSS, Chicago, IL, USA).

## Results

**General overview:** From February 2008 to February 2021, data from standardized quality control forms included in the medical records of 445 native kidney biopsies procedures were gathered. After excluding the patients submitted to renal mass biopsies, the remaining records were divided by age into two groups: group A, up to 18 y/o ( $n = 215$ ) and group B, over 18 y/o ( $n = 216$ ). Twenty-four patients (10 in group A and 14 in group B) underwent a second biopsy on a separate occasion due to inconclusive diagnosis on the first procedure.

No unexpected or unforeseen events that could affect the procedure were noted. Safe progression of the needle tip under sonographic guidance was completed in all cases. Flank elevation was sufficient to move the bowel medially, guaranteeing a safe pass of the biopsy needle to the cortex of the ipsilateral kidney, which was confirmed during the initial sonographic biopsy programming. Abdominal organ interposition between the needle trajectory and the native kidney was not observed and did not avert the biopsy in any of the cohorts. Despite a longer needle tract between the skin and the native kidney, no specific complications related to the technique were documented.

General anesthesia in the FF-SALP was performed safely in the pediatric and adult population when needed. The pediatric cohort had a higher need for general anesthesia (Table 2), but no differences were observed when comparing biopsy complications between groups (Table 2). A similar number of biopsies in the right and left kidney unites were performed in both cohorts (Table 2).

A laminar perinephric hematoma was observed in 16 patients and a subcapsular renal hematoma in two. No major complications were observed in the cohorts.

Less than 10 glomeruli in the biopsy samples or an inconclusive histopathological result was not associated with higher complication rates. Comparing the complication rates between patients that had  $> 10$  glomeruli in the biopsy samples to the patients that had  $< 10$  glomeruli, no differences were observed ( $16 (5.2\%)$  vs.  $3 (2.5\%)$ ;  $p = 0.3$ ,

respectively). Likewise, when complication rates between patients that had conclusive histopathological results were compared to the ones that had inconclusive results, no differences were observed (18 (4.4%) vs. 1 (4.2%);  $p = 1.0$ , respectively).

Overall, a similar number of cores were obtained in Groups A and B, but a significantly higher number of glomeruli was achieved in the pediatric cohort (Group A mean:  $20.6 \pm 12.3$ ,  $CI: 19.0\text{--}22.3$  vs group B mean:  $15.7 \pm 9.4$ ,

$CI: 14.5\text{--}17.00$ ;  $p < 0.001$ ) (Table 1, Figs. 3 and 4). Despite that, when looking at the minimum desirable cutoff limit of 10 glomeruli per biopsy and histopathologic yield, no differences were observed between the two groups (Table 2). Patient biopsy samples that had the optimal threshold of at least 10 glomeruli had a significantly higher rate of conclusive histopathological result (307 (99.4%) vs. 100 (82.0%);  $p < 0.0001$ ).

**Table 1** Patient Demographics, number of biopsy cores and number of glomeruli obtained comparing the two groups

|                | Group | <i>n</i> | Range        | Mean | SD   | <i>p</i>  |
|----------------|-------|----------|--------------|------|------|-----------|
| Age (years)    | A     | 215      | 0.5 to 18    | 9.9  | 4.4  |           |
|                | B     | 216      | 19 to 76     | 40.2 | 14.6 |           |
|                | Total | 431      |              |      |      |           |
| Height (m)     | A     |          | 0.59 to 1.77 | 1.33 | 0.26 |           |
|                | B     |          | 1.38 to 1.88 | 1.67 | 0.08 |           |
| Weight (kg)    | A     |          | 5.9 to 95    | 37.7 | 18.1 |           |
|                | B     |          | 31 to 108    | 67.9 | 13.0 |           |
| BMI            | A     |          | 10.3 to 36.7 | 19.6 | 4.5  | < 0.001*  |
|                | B     |          | 12.1 to 38.3 | 24.3 | 4.1  |           |
| # of cores     | A     |          | 2 to 5       | 2.4  | 0.66 | 0.020**   |
|                | B     |          | 2 to 5       | 2.5  | 0.66 |           |
| # of glomeruli | A     |          | 4 to 66      | 20.6 | 12.3 | < 0.001** |
|                | B     |          | 0 to 53      | 15.7 | 9.4  |           |

Group A: patients up to 18 years old. Group B: patients over 18 years old

\*ANOVA

\*\*Mann–Whitney Test

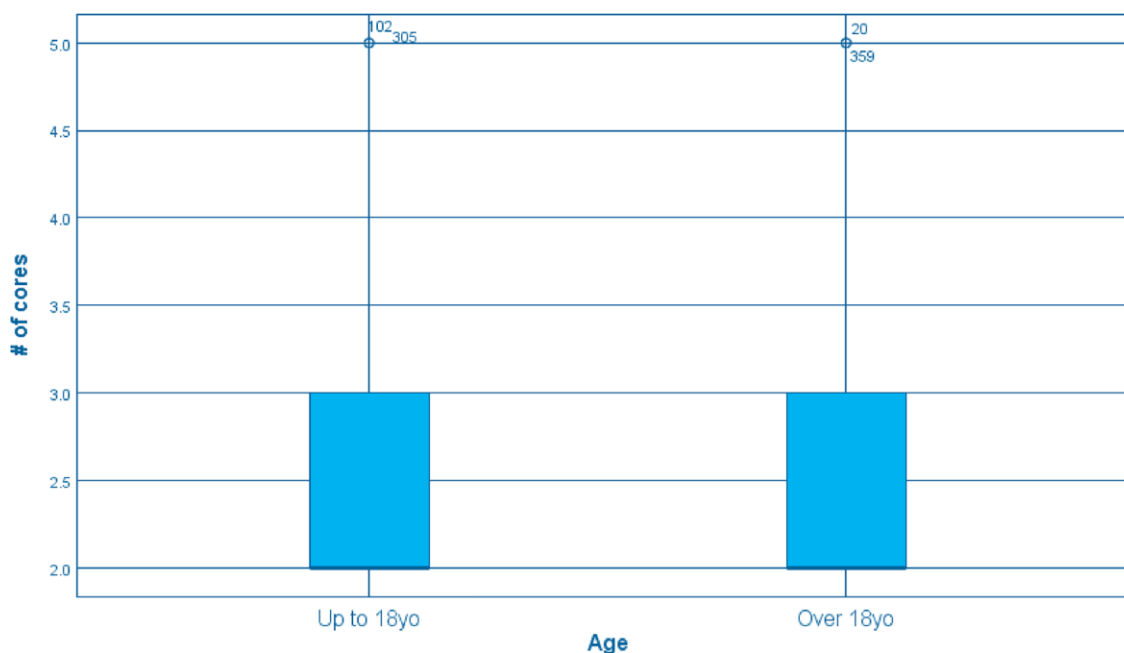


**Fig. 3** Box Plot graphic comparing the number of cores obtained per case in Group A (up to 18 y/o) and Group B (over 18 y/o). # of cores: total number of cores obtained by case

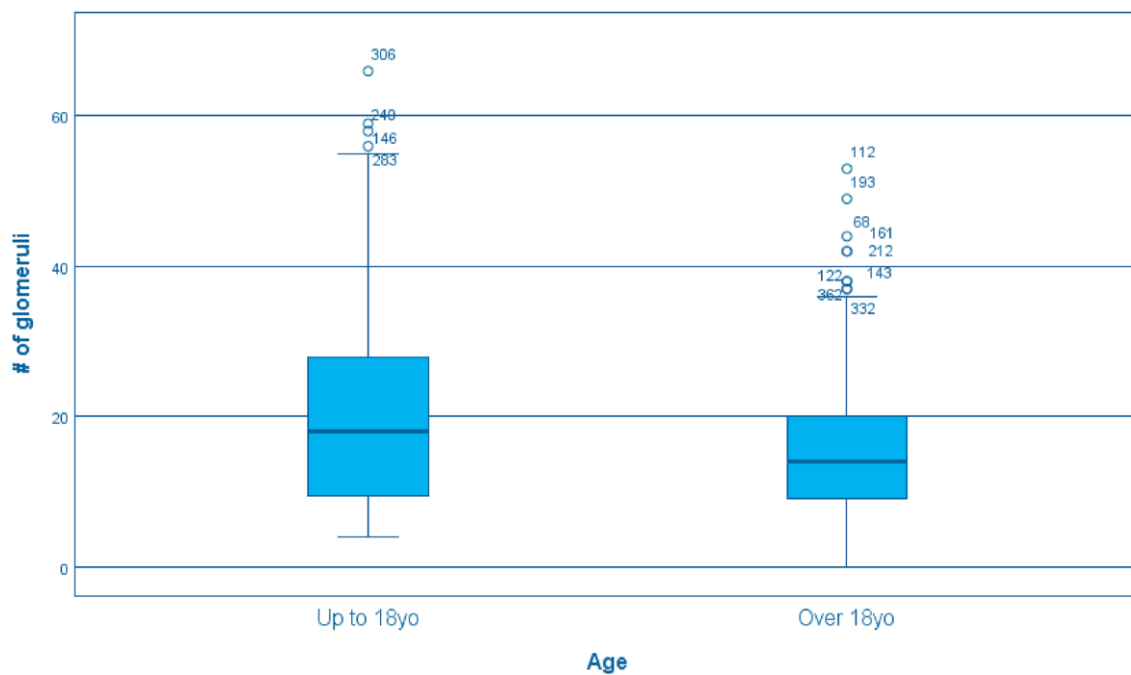


**Fig. 4** Box Plot graphic of the total number of glomeruli obtained per case in Group A (up to 18 y/o) and Group B (over 18 y/o). # of glomeruli: total number of glomeruli obtained by case

**Table 2** Results in obtaining at least 10 glomeruli, histopathologic conclusion, kidney side sampled and complications comparing groups A and B

|                            |              | Group          |               | P*      |
|----------------------------|--------------|----------------|---------------|---------|
|                            |              | Up to 18yo (A) | Over 18yo (B) |         |
| # Glomeruli                | < 10         | 51 (23.7%)     | 68 (31.5%)    | 0.072   |
|                            | ≥ 10         | 164 (76.3%)    | 148 (68.5%)   |         |
| Histopathologic conclusion | Insufficient | 10 (4.7%)      | 14 (6.5%)     | 0.408   |
|                            | Sufficient   | 205 (95.3%)    | 202 (93.5%)   |         |
| Kidney Sampled             | Right        | 203 (94.4%)    | 206 (95.4%)   | 0.653   |
|                            | Left         | 12 (5.6%)      | 10 (4.6%)     |         |
| Type of anesthesia         | General      | 115 (53.5%)    | 4 (1.9%)      | < 0.001 |
|                            | Local        | 100 (46.5%)    | 212 (98.1%)   |         |
| Complications              | No           | 186 (94.4%)    | 226 (96.3%)   | 0.454   |
|                            | Yes          | 12 (5.6%)      | 9 (3.7%)      |         |

Group A: patients up to 18 years old. Group B: patients over 18 years old

\* Chi-square test

Only 2 left kidneys sampled in group A had insufficient tissue for adequate histopathologic conclusion. The most common diagnosis in group A was minimal change disease and in group B, Focal segmental glomerulosclerosis. There was no influence in the type of anesthesia or kidney side biopsied when looking at the obtention of at least 10 glomeruli or histopathologic conclusion per case (Table 3). Also, kidney side sampled did not influence the obtention of sufficient material for histopathologic conclusion (Table 4). Only 2 left kidneys sampled in group A had insufficient tissue for adequate histopathologic conclusion.

**Table 3** Influence in the Type of Anesthesia in the obtention of at least 10 glomeruli and histopathologic conclusion per case

|                            |              | Group        |             | P*    |
|----------------------------|--------------|--------------|-------------|-------|
|                            |              | General      | Local       |       |
| # Glomeruli                | < 10         | 23 (19.3.0%) | 96 (30.8%)  | 0.018 |
|                            | ≥ 10         | 96 (80.7%)   | 216 (69.2%) |       |
| Histopathologic conclusion | Insufficient | 5 (4.2%)     | 19 (6.1%)   | 0.445 |
|                            | Sufficient   | 114 (95.8%)  | 293 (93.9%) |       |

\*Chi-square test

**Table 4** Influence in kidney side biopsied in the obtention of histopathologic result

|                            |     | Kidney      |            | <i>P</i> * |
|----------------------------|-----|-------------|------------|------------|
|                            |     | Right       | Left       |            |
| Histopathologic conclusion | No  | 22 (5.4%)   | 2 (9.1%)   | 0.350      |
|                            | Yes | 387 (94.6%) | 20 (90.9%) |            |

\*Fisher's Exact Test

## Discussion

Due to its advantages, ultrasound-guided biopsy of native kidneys in FF-SALP has been routinely performed in our service since 2006, both in children and adults. However, a specific evaluation of its application in children has not yet been conducted in the literature.

Considering the pediatric patient, ultrasound-guided renal biopsy via the posterior access has some limitations. In a significant number of cases general anesthesia is required. Positioning the patient in prone decubitus for biopsy may prove demanding, as it involves orotracheal intubation, mechanical ventilation, and repositioning the patient from dorsal to ventral decubitus, which increases the risks of the procedure.

In contrast, biopsy in SALP allows easier access to the airways, no patient repositioning after anesthesia, and is better tolerated. Patients with respiratory or hemodynamic restrictions also benefit from biopsies in SALP since anesthesia in the PP complicates ventilatory management and interferes with various bodily functions and drug effects [14]. It should be noted that although not necessary in every case, general anesthesia for USPB in children has proven faster and smoother than with local anesthesia [15].

In our experience, performing renal biopsies in SALP offers an excellent sonographic window to the native kidneys and at the same time, allows access to the patient's airways by the anesthetist, facilitating the procedure under general anesthesia with the use of a laryngeal mask or even intravenous sedation. On the other hand, in our experience, renal biopsy in PP does not offer the best angles for sonographic visualization of the biopsy needle as compared to the SALP.

In our hands USPB in FF-SALP of native kidney units of children and adults proved safe and effective, with no unforeseen events or major complications. Considering USPB in SALP, Enríquez Et al. demonstrated minor complication rates of 4.4% and no major complications [12]. Gesualdo Et al. reported 11.8% complication rates related to bleeding, all of which were mild and of little significance, except for a single case of arteriovenous fistula [13]. No significant differences were reported regarding the diagnostic yield, complications, or post-biopsy pain in SALP [12, 13]. Using the same criteria, our study

demonstrated comparable complication rates to those reported in the literature for renal biopsies in children and adults, either in PP and or SALP, but with no major complications [3].

Compared with previous studies, Enríquez et al. [12] and Gesualdo et al. [13] used automatic 16G needles to perform biopsies in SALP in native adult kidneys using a free-hand technique. Our study used semi-automatic 18G needles in both adults and children, with no detriment in diagnostic yield or increase in complications, compared to the literature. Semi-automatic needles have a lighter cutting impact during projection of the TRU-CUT mechanism, which may be a safer choice for pediatric biopsies. Additionally, they allow for retraction and repositioning of the needle cutting mechanism before the final sample is acquired, providing additional safety to the biopsy.

Traditionally, biopsy fragments are obtained at the lower pole of the kidney, in the sagittal axis of the unit, either in the craniocaudal or caudocranial direction. Other authors have used the axial plane of the lower pole as the site of biopsy [16, 17]. In this study fragments were obtained from the middle third of the native kidney in the axial plane, either on the anterior or posterior aspect of the selected renal unit, since this region tends to offer the greatest transverse diameter of cortex for core optimization (Fig. 2). We did not observe an increase in complications with this approach. Interestingly, despite using the same 18G needles, and a similar number of cores in both cohorts, we observed a higher number of glomeruli in tissue samples of the pediatric population (Table 1 and Fig. 3).

Unlike most but not all authors, only the physician in charge of the procedure handled the transducer and the biopsy needle. In our opinion, during insonation, the biopsy needle tip should be perfectly characterized to reduce the risk of injury to adjacent structures. Often, a sonographic cutting image of the needle's body can mimic its tip, and concurrent handling of the transducer and needle by the same operator reduces this type of technical mistake.

Ultrasound Kidney biopsy in a 90° decubitus has also been described [18, 19]. Towbin et al. had children positioned in the full lateral decubitus with a bolster at the waist, to increase the distance between the contralateral costal margin and the iliac crest [18]. Biopsies were performed in children either under sedation or general anesthesia using a 15G needle in the oblique transverse plane [18]. It is known that raising the ipsilateral flank above 45 degrees promotes medial mobilization of the native kidney [20], increasing the distance from the skin to the renal unit and hence, path of the needle to be traveled during biopsy. Furthermore, ventilation in the full lateral decubitus with a bolster at the waist may also prove challenging, especially in smaller children.

Tse et al. [19] performed a series of ultrasound kidney biopsies in children also in the lateral position. This

technique proved to be a valid alternative for biopsies in children undergoing general anesthesia [19]. Nonetheless, the posterior access for the biopsy needle described in lateral decubitus resembles those of the procedure in the PP. In our experience, ultrasound-guided kidney biopsy in the FF-SALP offers the best angles for sonographic visualization of the biopsy needle and the renal unit at the same time, as both structures will be insonated in a perpendicular fashion. Moreover, the 90° lateral position would not be suitable for the use of a laryngeal mask for general anesthesia and in this scenario, orotracheal intubation would be mandatory.

Finally, kidney biopsy in the SALP proposed in this article, using two cushions interspersed with a Free-Flank (FF-SALP), offers a wider range of possibilities for percutaneous introduction of the biopsy needle, eliminating the need for excessive elevation of the patient's ipsilateral flank. More importantly, for biopsies under general anesthesia, it offers advantages in terms of airway management, making it particularly valuable for pediatric patients requiring general anesthesia. In our opinion, this technique should be considered the standard for pediatric patients, especially when general anesthesia is necessary. To our knowledge, this is the first time that ultrasound-guided kidney biopsy in FF-SALP was reported for pediatric patients.

Some limitations of this study must be emphasized. Considering the FF-SALP as a less common approach for ultrasound-guided native kidney biopsies, a prospective randomized comparative non-inferiority trial directly assessing FF-SALP with PP would be necessary to validate this new approach as equivalent in terms of safety and effectiveness. Another limitation is the monocenter, retrospective design, which may limit its external validity. More studies demonstrating reproducibility may be needed to support our results.

## Conclusions

USPB of native kidneys in the FF-SALP position is a safe and effective method for tissue sampling in patients with parenchymal disease. It demonstrated comparable diagnostic yields and complication rates in the pediatric and adult populations. Additionally, it provides advantages in terms of airway management, making it particularly useful for pediatric patients that require general anesthesia.

**Funding** No external funding was secured for this study.

## Declarations

**Conflict of interest** Authors disclose no financial or non-financial interests that are directly or indirectly related to this work submitted for publication.

**Ethical approval** This study was approved by the Institutional Review Board of the Santa Casa de Misericórdia de São Paulo.

## References

1. Cameron S, Hicks J (1997) The introduction of renal biopsy into nephrology from 1901 to 1961: a paradigm of the forming of nephrology by technology. *Am J Nephrol* 17:347–358. <https://doi.org/10.1159/000169122>
2. Whittier WL, Korbet SM (2004) Timing of complications in percutaneous renal biopsy. *Journal of the American Society of Nephrology* 15:142–147. <https://doi.org/10.1097/01.ASN.0000102472.37947.14>
3. Visconti L, Cernaro V, Ricciardi CA, et al (2016) Renal biopsy: still a landmark for the nephrologist. *World J Nephrol* 5:321. <https://doi.org/10.5527/wjn.v5.i4.321>
4. Bandari J, Fuller TW, Turner I RM, D'Agostino LA (2016) Renal biopsy for medical renal disease: indications and contraindications. *Can J Urol* 23:8121–6
5. Gauthier BG, Mahadeo RS, Trachtman H (1993) Techniques for percutaneous renal biopsies. *Pediatric Nephrology* 7:457–463. <https://doi.org/10.1007/BF00857575>
6. Uppot RN, Harisinghani MG, Gervais DA (2010) Imaging-guided percutaneous renal biopsy: rationale and approach. *American Journal of Roentgenology* 194:1443–1449
7. Santangelo L, Netti GS, Giordano P, et al (2018) Indications and results of renal biopsy in children: a 36-year experience. *World Journal of Pediatrics* 14:127–133. <https://doi.org/10.1007/s12519-018-0147-5>
8. Hunter RW, Ramaswamy R, Patel D, Dhaun N (2017) Ultrasound-guided renal biopsy. *Br J Hosp Med* 78:C56–C59. <https://doi.org/10.12968/hmed.2017.78.4.C56>
9. Mantan M, Batra V (2020) Renal biopsy in children. *Indian Pediatr* 57:452–458
10. Franke M, Kramarczyk A, Taylan C, et al (2014) Ultrasound-guided percutaneous renal biopsy in 295 children and adolescents: role of ultrasound and analysis of complications. *PLoS One* 9. <https://doi.org/10.1371/journal.pone.0114737>
11. Feneberg R, Schaefer F, Zieger B, et al (1998) Percutaneous Renal Biopsy in Children: A 27-Year Experience. *Nephron* 79:438–446. <https://doi.org/10.1159/000045090>
12. Enríquez R, Martínez M, Amorós F, et al (2003) Evaluation of the oblique supine position for percutaneous renal biopsy. *Nefrologia* 23:160–4
13. Gesualdo L, Cormio L, Stallone G, et al (2008) Percutaneous ultrasound-guided renal biopsy in supine antero-lateral position: a new approach for obese and non-obese patients. *Nephrology Dialysis Transplantation* 23:971–976. <https://doi.org/10.1093/ndt/gfm669>
14. Pump B, Talleruphuus U, Christensen NJ, et al (2002) Effects of supine, prone, and lateral positions on cardiovascular and renal variables in humans. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology* 283:R174–R180. <https://doi.org/10.1152/ajpregu.00619.2001>
15. Olowu WA (2006) Local Versus General Anesthesia in Pediatric Renal Biopsy: Which is Associated With Better Outcome? *Saudi J Kidney Dis Transpl* 17:25–33

16. 17. Prasad N, Shukla R, Behera M, et al (2020) Comparison of yield and complications of craniocaudal versus caudocranial needle trajectory for kidney biopsy. *Journal of Vascular Access* 21:73–78. <https://doi.org/10.1177/1129729819854009>
17. 18. Shamshirgar F, Bagheri SM (2017) Percutaneous ultrasound-guided renal biopsy; a comparison of axial vs. sagittal probe location. *Rom J Intern Med* 55:96–102. <https://doi.org/10.1515/rjim-2017-0011>
18. 19. Towbin RB, Amundson GM, Fleischmann LE, et al (1991) Real-time us guidance during renal biopsy in children: a different approach. *Journal of Vascular and Interventional Radiology* 2:561–562. [https://doi.org/10.1016/S1051-0443\(91\)72243-4](https://doi.org/10.1016/S1051-0443(91)72243-4)
19. 20. Tse Y, Yadav P, Herrema I, et al (2013) Performing renal biopsies in children under general anaesthesia in the lateral position. *Pediatric Nephrology* 28:671–673. <https://doi.org/10.1007/s00467-012-2388-1>
20. 21. URJA JGV, GERHOLD JV, LOPEZ JAL, et al (1998) Technique and complications of percutaneous nephroscopy: experience with 557 patients in the supine position. *Journal of Urology* 160:1975–1978. [https://doi.org/10.1016/S0022-5347\(01\)62217-1](https://doi.org/10.1016/S0022-5347(01)62217-1)

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#### **4.2. Artigo 2: O artigo a seguir foi publicado na revista CUREUS**

# Glomerular Yield in Ultrasound-Guided Native Kidney Biopsies in Pediatric and Adult Populations With Age-Stratified Subgroups

Review began 08/02/2025  
Review ended 08/25/2025  
Published 08/28/2025

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DOI: 10.7759/cureus.91202

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## Abstract

**Background:** This study compares the glomerular yield, mean number of biopsy cores, and complication rates between pediatric and adult populations undergoing ultrasound-guided native kidney biopsies. Additionally, the adult population was stratified into subgroups to further analyze age-related differences in glomerular yield and complication rates.

**Materials and methods:** A retrospective cohort study was conducted using data from 431 native kidney biopsies performed between February 2008 and February 2021. Patients were divided into two main groups: pediatric ( $\leq 18$  years old,  $n = 215$ ) and adult ( $> 18$  years old,  $n = 216$ ). Adult patients were further stratified into three subgroups: those aged  $> 18$  to 40 years old ( $n = 108$ ),  $> 40$  to 60 years old ( $n = 72$ ), and  $> 60$  years old ( $n = 36$ ).

**Results:** Pediatric patients had a higher mean number of glomeruli per core than adults ( $20.6 \pm 12.3$  vs.  $15.7 \pm 9.4$ ;  $p < 0.001$ ). Among adults, yield declined with age:  $7.2 \pm 9.8$  ( $> 18$ -40 years),  $15.1 \pm 9.1$  ( $> 40$ -60 years), and  $13.8 \pm 8.7$  ( $> 60$  years) ( $p < 0.05$ ). No difference in core numbers between pediatric and adults ( $2.4 \pm 0.66$  vs.  $2.5 \pm 0.66$ ;  $p = 0.08$ ) or among adult subgroups was observed. In the adult stratification group, the  $> 18$  to 40-year-old subgroup had the highest mean number of glomeruli ( $17.2 \pm 9.8$ ), followed by the  $> 40$  to 60-year-old ( $15.1 \pm 9.1$ ) and  $> 60$ -year-old subgroups ( $13.8 \pm 8.7$ ) ( $p < 0.05$ ). Complication rates were low across all groups, with no significant differences observed between the pediatric and adult populations (12/215, 5.6% vs. 8/216, 3.7%;  $p = 0.454$ ). Among the adult subgroups, the  $> 18$  to 40-year-old subgroup had the lowest complication rate (3/108, 2.8%), followed by the  $> 40$  to 60-year-old (3/72, 4.2%) and  $> 60$ -year-old subgroups (2/36, 5.6%). However, these differences were not statistically significant ( $p = 0.512$ ).

**Conclusions:** Pediatric patients exhibit a higher glomerular yield per biopsy core compared to adults, with no significant difference in the number of biopsy cores obtained. Among adults, younger patients ( $> 18$  to 40 years) demonstrate a higher glomerular yield compared to older age groups, suggesting that age may influence glomerular density and biopsy outcomes. Complication rates were low across all age groups, with no significant differences observed. These findings highlight the importance of considering age-related factors when performing native kidney biopsies to optimize diagnostic yield and minimize complications.

**Categories:** Radiology, Nephrology, Pediatrics

**Keywords:** adult, biopsy cores, children, complications, glomerular density, glomerular yield, native kidney, pediatric, percutaneous, ultrasound-guided biopsy

## Introduction

Native kidney biopsy is a cornerstone diagnostic procedure in nephrology, providing histopathological insights that inform diagnosis, prognosis, and treatment strategies for a wide range of renal diseases [1-3]. Since its introduction, the technique has undergone significant evolution, with ultrasound-guided percutaneous biopsy emerging as the gold standard due to its safety, efficacy, and ability to yield adequate renal tissue for analysis [4,5].

One of the most important determinants of a successful kidney biopsy is the glomerular yield, defined as the number of glomeruli obtained in the biopsy samples. Adequate glomerular yield is essential for accurate histopathological diagnosis, with a minimum of 10 glomeruli per sample considered optimal for reliable interpretation [6].

The diagnostic utility of kidney biopsies, however, is influenced by several factors, including patient age, renal anatomy, and comorbid conditions. While previous studies have compared biopsy outcomes between pediatric and adult populations, there is limited research on how age-related factors within the adult population influence glomerular yield and complication rates. Age-related changes in renal structure, such as glomerulosclerosis, interstitial fibrosis, and reduced glomerular density, are well-documented and may

### How to cite this article

Ravizzini P C, Lino H A, de Faria Castro Fleury E, et al. (August 28, 2025) Glomerular Yield in Ultrasound-Guided Native Kidney Biopsies in Pediatric and Adult Populations With Age-Stratified Subgroups. Cureus 17(8): e91202. DOI 10.7759/cureus.91202

impact biopsy outcomes [7,8]. Additionally, the prevalence of comorbid conditions like hypertension and diabetes, which are more common in older adults, may further complicate biopsy procedures and outcomes [9].

This study aims to address existing gaps by comparing the mean number of biopsy cores, glomeruli per core, and complication rates between pediatric populations ( $\leq 18$  years) and adult populations ( $> 18$  years). Additionally, it seeks to stratify the adult population into subgroups ( $> 18$  to 40,  $> 40$  to 60, and  $> 60$  years) to investigate how age-related variations in glomerular yield may influence diagnostic adequacy, thereby providing insights for optimizing biopsy protocols across different age groups.

## Materials And Methods

This retrospective cohort study evaluated 431 consecutive ultrasound-guided native kidney biopsies performed at the Interventional Radiology Service of Santa Casa de Misericórdia de São Paulo, Brazil, between February 2008 and February 2021. Patients were divided into two main groups: pediatric ( $\leq 18$  years,  $n = 215$ ) and adult ( $> 18$  years,  $n = 216$ ). The adult group was further stratified into three age-based subgroups:  $> 18$ -40 years ( $n = 108$ ),  $> 40$ -60 years ( $n = 72$ ), and  $> 60$  years ( $n = 36$ ). Exclusion criteria included biopsies of transplanted kidneys, incomplete procedural records, or insufficient tissue for histopathological analysis.

All biopsies were performed by a single interventional radiologist under real-time ultrasound guidance using an Envisor C HD or Affiniti 70 device (Philips Ultrasound Inc., Bothell, WA), with a 3.5-5 MHz convex transducer. Patients were positioned in the free-flank supine anterolateral decubitus, as previously described [10]. A semi-automatic 18-gauge needle (SuperCore II, Argon Medical, Frisco, TX) was used to obtain at least two cores per biopsy. Additional passes were performed if initial samples were deemed inadequate based on tissue length less than 1 cm.

For glomerular yield quantification, biopsy cores were fixed in 10% formalin, embedded in paraffin, and sectioned at a thickness of 2-3  $\mu\text{m}$ . Tissue sections were stained with hematoxylin and eosin (H&E), periodic acid-Schiff (PAS), and Masson's trichrome. A renal pathologist blinded to the clinical data counted the number of intact glomeruli per core under light microscopy at  $\times 200$  magnification, excluding those that were globally sclerotic.

Primary outcomes included the mean number of glomeruli per core (total glomeruli divided by the number of cores) and the proportion of biopsies achieving the diagnostic threshold of  $\geq 10$  glomeruli [6]. A biopsy core was considered non-optimal if it measured less than 1.0 mm in length or contained fewer than ten glomeruli. Secondary outcomes were the mean number of biopsy cores per procedure and complication rates, categorized as major or minor as presented in Gesualdo et al. and Visconti et al. [2,11].

Statistical analysis was performed using SPSS Statistics version 25.0 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Continuous variables were expressed as mean  $\pm$  standard deviation (SD), and categorical variables as frequencies. The Mann-Whitney U test was used to compare glomerular yield and core counts between pediatric and adult groups. Differences among adult age subgroups were assessed using ANOVA with post-hoc Tukey tests. Complication rates and diagnostic adequacy were analyzed using the chi-square test. A p-value  $< 0.05$  was considered statistically significant. The study was approved by the Institutional Review Board of Santa Casa de Misericórdia de São Paulo (approval number: 48707221.4.0000.5479).

## Results

Demographic data are depicted in Table 1. The pediatric group had a significantly higher mean number of glomeruli per biopsy core compared to the adult group (Table 2); however, there was no significant difference in the mean number of biopsy cores between the pediatric and adult groups ( $2.4 \pm 0.66$  vs.  $2.5 \pm 0.66$ ;  $p = 0.08$ ). Overall complication rates were low, and no differences were observed between the children and adult groups (Table 3).

| Age group (years) | n   | Mean age (years ± SD) | Age range (years) | Mean BMI (kg/m² ± SD) | BMI range (kg/m²) | p-value (BMI) | Test statistic |
|-------------------|-----|-----------------------|-------------------|-----------------------|-------------------|---------------|----------------|
| Pediatric (≤18)   | 215 | 10.5 ± 4.2            | 1-18              | 18.3 ± 3.1            | 12.0-24.5         | <0.001*       | F = 15.7       |
| Adult subgroups   |     |                       |                   |                       |                   |               |                |
| >18 to 40         | 108 | 29.7 ± 6.5            | 18.1-40           | 24.5 ± 4.2            | 16.8-35.2         | NA            | N-A            |
| >40 to 60         | 72  | 50.3 ± 5.8            | 40.1-60           | 27.8 ± 5.1            | 18.6-38.4         | NA            | N-A            |
| >60               | 36  | 68.4 ± 6.2            | 60.1-85           | 28.6 ± 4.9            | 20.5-39.7         | NA            | N-A            |

TABLE 1: Demographic characteristics of the study population

\* ANOVA was used for BMI comparison between pediatric and adult groups.

ANOVA: analysis of variance, BMI: body mass index, SD: standard deviation, NA: not analyzed, N-A: not applicable

| Group           | n   | Range (glomeruli) | Mean glomeruli | SD   | p-value           | Test statistic |
|-----------------|-----|-------------------|----------------|------|-------------------|----------------|
| Pediatric (≤18) | 215 | 4-66              | 20.6           | 12.3 | <0.001*           | U = 18,542     |
| Adult (overall) | 216 | 0-53              | 15.7           | 9.4  | Reference         | N-A            |
| Adult subgroups |     |                   |                |      |                   |                |
| >18 to 40 years | 108 | 1-53              | 17.2           | 9.8  | <0.05† (vs. >60)  | F = 4.32       |
| >40 to 60 years | 72  | 0-44              | 15.1           | 9.1  | 0.08 (vs. >18-40) | t = 1.76       |
| >60 years       | 36  | 0-37              | 13.8           | 8.7  | 0.03 (vs. >18-40) | t = 2.21       |

TABLE 2: Mean number of biopsy cores and glomeruli obtained per case

\* Mann-Whitney U test for pediatric vs. adult comparison, † ANOVA with post-hoc t-tests for adult subgroups

SD: standard deviation, N-A: not applicable

| Age group (years) | n   | Complication rate | p-value (complications) | Test statistic | Inconclusive results | p-value (inconclusive) | Test statistic |
|-------------------|-----|-------------------|-------------------------|----------------|----------------------|------------------------|----------------|
| Pediatric (≤18)   | 215 | 12 (5.6%)         | 0.454*                  | χ² = 0.56      | 45 (20.9%)           | 0.021*                 | χ² = 5.32      |
| Adult (>18)       | 216 | 8 (3.7%)          | Reference               | N-A            | 38 (17.6%)           | Reference              | Not applicable |
| Adult subgroups   |     |                   |                         |                |                      |                        |                |
| >18 to 40         | 108 | 3 (2.8%)          | 0.823† (vs. >40-60)     | χ² = 0.05      | 15 (13.9%)           | 0.038† (vs. >60)       | χ² = 4.29      |
| >40 to 60         | 72  | 3 (4.2%)          | 0.823† (vs. >60)        | χ² = 0.05      | 12 (16.7%)           | 0.823† (vs. >18-40)    | χ² = 0.05      |
| >60               | 36  | 2 (5.6%)          | 0.454† (vs. >18-40)     | χ² = 0.56      | 11 (30.6%)           | 0.003† (vs. >18-40)    | χ² = 8.76      |

TABLE 3: Complication rates and inconclusive results by age group

\* Chi-square test for pediatric vs. adult comparisons, † Chi-square or Fisher's exact test for adult subgroup comparisons

N-A: not applicable

The mean number of biopsy cores also did not differ significantly when comparing the adult age-stratified subgroups ( $p = 0.12$ ). Among the subgroups, the >18 to 40-year-old subgroup had the highest number of glomeruli per core, followed by the >40 to 60-year-old and the >60-year-old subgroups (Table 2). When comparing the mean number of glomeruli in the >18 to 40-year-old and >40 to 60-year-old subgroups and the >40 to 60-year-old and >60-year-old subgroups, no statistical significance was found (Table 2). The >60-year-old subgroup had significantly fewer glomeruli per core compared to the >18 to 40-year-old subgroup (Table 2). Complication rates and the inconclusive histopathological results are shown in Table 3.

The proportion of biopsy samples containing at least 10 glomeruli was higher in the pediatric group compared to the adult group (164/215, 76.3% vs. 148/216, 68.5%;  $p = 0.072$ ). Among the adult subgroups, the >18 to 40-year-old subgroup had the highest proportion of samples with  $\geq 10$  glomeruli (78/108, 72.2%), followed by the >40 to 60-year-old subgroup (48/72, 66.7%) and the >60-year-old subgroup (22/36, 61.1%).

In the pediatric group ( $n = 215$ ), the most prevalent conditions were focal segmental glomerulosclerosis (69/215, 32.1%), followed by minimal histological lesion (55/215, 25.6%) and proliferative mesangial glomerulonephritis (39/215, 18.3%). In the >18 to 40-year-old subgroup ( $n = 108$ ), segmental and focal glomerulosclerosis was the most common diagnosis (31/108, 28.7%), followed by membranous glomerulonephritis (24/108, 22.4%) and proliferative mesangial glomerulonephritis (21/108, 19.8%). In the >40 to 60-year-old subgroup ( $n = 72$ ), segmental and focal glomerulosclerosis remained the leading condition (22/72, 30.2%), followed by membranous glomerulonephritis (18/72, 25.6%) and diabetic nephrosclerosis (14/72, 18.9%). In the >60-year-old subgroup ( $n = 36$ ), segmental and focal glomerulosclerosis was again the most frequent diagnosis (13/36, 35.4%), while diabetic nephrosclerosis (10/36, 28.3%) and membranous glomerulonephritis (7/36, 20.1%) were also observed. Segmental and focal glomerulosclerosis consistently emerged as a predominant condition in all cohorts.

## Discussion

This study demonstrates that pediatric patients exhibit a higher glomerular yield per biopsy core compared to adults (Table 2), which may be attributed to differences in glomerular density and renal parenchymal characteristics between these populations. The lack of a significant difference in the number of biopsy cores suggests that the higher glomerular yield in pediatric patients is not due to a greater number of cores but rather to the quality of the tissue obtained. These results align with studies showing that younger patients have higher glomerular density, which declines with age due to factors such as hypertension, diabetes, and other age-related renal changes [7,12].

Adequate glomerular yield is essential for adequate interpretation of biopsy samples, with a minimum of 10 glomeruli per sample generally considered optimal [6]. However, achieving this yield can be challenging, particularly in older adults or patients with advanced renal disease, where glomerulosclerosis and interstitial fibrosis are more prevalent [7,8]. Additionally, certain conditions may result in fewer intact glomeruli being available for sampling. For instance, diabetic nephrosclerosis or advanced glomerulosclerosis may result in lower glomerular counts, complicating the diagnostic process [7,8].

Additional considerations can also be drawn regarding the technique and equipment used during the biopsy procedures. Typically, the same biopsy needle gauge (e.g., 18 G) is used for both pediatric and adult patients, which may not always be ideal. While 18-G needles are generally safe and effective, they may not yield sufficient tissue, particularly in older adults or patients with dense renal fibrosis. Conversely, larger-gauge needles (e.g., 16 G) may yield more glomeruli but could increase the risk of complications, especially in pediatric patients or those with fragile renal tissue [13]. This uniform approach to biopsy technique and needle selection may contribute to variations in complication rates and diagnostic yield across different age groups and disease types.

The primary goal of ultrasound-guided native kidney biopsies is to obtain adequate biopsy samples with minimal complication rates. However, this balance is crucial, as inadequate sampling can lead to inconclusive results, necessitating repeat biopsies and increasing patient risk. On the other hand, excessive tissue sampling or the use of larger-gauge needles may increase the likelihood of complications such as bleeding or hematoma, particularly in older adults or those with comorbid conditions like hypertension or diabetes [13,14]. Therefore, optimizing technique while minimizing risks remains a key focus in ultrasound-guided native kidney biopsies. This paper provides a comprehensive analysis of glomerular yield and complication rates in native kidney biopsies across pediatric and adult populations. The results obtained underscore the importance of considering age-related factors when performing kidney biopsies to optimize diagnostic yield and minimize complications.

The lack of difference in the number of biopsy cores between adult and pediatric groups suggests that the higher yield in pediatric patients is not due to a greater number of cores but instead to the higher glomerular density of the tissue obtained. In fact, fewer age-related structural changes in the kidneys of younger patients may favor a higher glomerular density [7,12]. This suggests that pediatric patients may require fewer cores to achieve an adequate diagnostic yield, potentially reducing procedural time and associated risks.

Table 2 further stratifies the adult population into age subgroups, revealing a progressive decline in glomerular yield with age. The mean number of glomeruli was slightly lower when comparing the >18 to 40-year-old subgroup to the >40 to 60-year-old subgroup, but the difference was not significant ( $p = 0.08$ ). Between the >40 to 60-year-old subgroup and the >60-year-old subgroup, the difference was also not significant ( $p = 0.25$ ), although the trend showed a further reduction in glomerular yield. The >60-year-old subgroup had significantly fewer glomeruli compared to the >18 to 40-year-old subgroup ( $p = 0.03$ ). Those findings suggest an age-related gradual decline in glomeruli count with age, with the most pronounced difference occurring after 60 years. In fact, age-related changes in renal structure, such as glomerulosclerosis and interstitial fibrosis, have been demonstrated to contribute to lower glomerular density in older adults [7,8], coupled with a decline in the natural reduction in glomerular filtration rate that occurs with aging [9]. Therefore, younger adults (>18 to 40 years) may have more favorable biopsy outcomes and a higher glomerular yield, while older adults, particularly those over 60, may require additional considerations to optimize diagnostic yield.

Complication rates were low across all age groups, with no significant differences observed between pediatric and adult populations (Table 3). Among the adult subgroups, the >18 to 40-year-old subgroup had the lowest complication rate, followed by the >40 to 60-year-old subgroup and the >60-year-old subgroup (Table 3). Although these differences were not statistically significant, the slightly higher complication rate in the >60-year-old subgroup may be correlated with age-related vascular fragility and comorbid conditions, which are more prevalent in older adults [14]. Nevertheless, these findings suggest that percutaneous renal biopsies are generally safe when performed with real-time ultrasound guidance, even in older patients, as previously shown [13,15]. However, the slightly higher complication rate in older adults underscores the need for careful management of comorbid conditions to minimize risks.

Variations in inconclusive histopathological results across age groups are depicted in Table 3. The pediatric group had a slightly higher prevalence of inconclusive results compared to the overall adult population (Table 3). This may reflect technical challenges in obtaining adequate tissue samples in younger patients, despite their higher glomerular density. Among the adult subgroups, the >60-year-old subgroup had the highest prevalence of inconclusive results (11/36, 30.6%), which aligns with the decline in glomerular yield in older age groups but may also relate to age-related structural changes in the kidney, as well as comorbid conditions that compromise renal tissue integrity [7,8]. Hence, age-specific strategies could be implemented to optimize biopsy outcomes, particularly in older adults and pediatric patients, thereby reducing the likelihood of inconclusive results and improving diagnostic accuracy.

The findings in this study collectively highlight the importance of considering age-related factors when performing native kidney biopsies. Pediatric patients exhibit a higher glomerular yield per biopsy core, which may reduce the need for multiple cores. In contrast, older adults, particularly those over 60, may require additional considerations to optimize diagnostic yield and minimize complications. The use of larger-gauge needles (e.g., 16 G) may be beneficial in patients requiring a higher diagnostic yield, as suggested by previous studies [13]. However, in older adults or those at higher risk of complications, the use of 18-G needles may be more appropriate to balance diagnostic yield with safety [14]. Additionally, managing comorbid conditions such as hypertension and diabetes in older adults may improve biopsy outcomes by reducing the risk of inconclusive results and complications [13,14]. Nevertheless, advanced age alone should not deter clinicians from performing kidney biopsies in older adults, as the procedure remains both safe and effective, with adequate glomerular yield in elderly patients over 65 years [15].

This study has several important implications for clinical practice. First, the higher glomerular yield in pediatric patients suggests fewer biopsy cores may be needed to achieve an adequate diagnostic yield, potentially reducing procedural time and risks. For older adults, particularly those over 60, the lower glomerular yield underscores the importance of careful planning and potentially additional cores to ensure sufficient tissue for accurate diagnosis. Clinicians should also consider the type of kidney disease when performing biopsies, as certain conditions may affect glomerular density and yield.

However, this study has several limitations that should be acknowledged. First, it is a single-center, single-operator study, as the same interventional radiologist performed all biopsies. While this approach ensures consistency in technique, it may limit the generalizability of the findings, as operator experience and institutional protocols can influence biopsy outcomes. Future multi-center studies involving multiple operators would provide a more comprehensive understanding of how these factors impact glomerular yield and complication rates. While no statistically significant differences in complication rates were found between pediatric and adult populations, a slightly higher rate of complications was observed in children (5.6% vs. 3.7%). This finding may still be clinically relevant, particularly given the higher glomerular density in pediatric patients. It may be worth considering the use of smaller-gauge needles in children to reduce the risk of complications, as their higher glomerular density may allow for adequate diagnostic yield with fewer risks [13]. Although we adjusted for common comorbidities, the impact of specific renal pathologies (e.g., diabetic nephropathy or amyloidosis) on glomerular yield was not separately analyzed due to sample size constraints. Future studies could explore disease-specific effects in larger cohorts.

## Conclusions

This study demonstrates that pediatric patients exhibit a higher glomerular yield per biopsy core compared to adults. Biopsies in younger adults also demonstrated a higher glomerular yield compared to older age groups, suggesting that age may influence glomerular density and the outcomes of biopsies. These findings highlight the importance of considering age-related factors when performing native kidney biopsies to optimize diagnostic yield and minimize complications. Future studies should explore the impact of comorbid conditions, biopsy techniques, and needle size on biopsy outcomes, particularly in older adults and pediatric patients.

## Additional Information

### Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

**Concept and design:** Pedro C. Ravizzini, Henrique A. Lino, Eduardo de Faria Castro Fleury, Luis Gustavo M. Toledo

**Acquisition, analysis, or interpretation of data:** Pedro C. Ravizzini, Henrique A. Lino, Eduardo de Faria Castro Fleury, Luis Gustavo M. Toledo

**Drafting of the manuscript:** Pedro C. Ravizzini

**Critical review of the manuscript for important intellectual content:** Pedro C. Ravizzini, Henrique A. Lino, Eduardo de Faria Castro Fleury, Luis Gustavo M. Toledo

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### Disclosures

**Human subjects:** Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Institutional Review Board of Santa Casa de Misericórdia de São Paulo issued approval 48707221.4.0000.5479. This study utilizes the same patient cohort previously approved by the Research Ethics Committee (report number: 5.122.737) but presents a novel analysis. It approaches histopathology, emphasizing the importance of considering age-related factors when performing native kidney biopsies to optimize diagnostic yield and minimize complications. All data were reanalyzed using a distinct methodological approach, yielding original findings not previously reported in prior publications.

**Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue.

**Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

## References

1. Cameron JS, Hicks J: The introduction of renal biopsy into nephrology from 1901 to 1961: a paradigm of the forming of nephrology by technology. *Am J Nephrol.* 1997, 17:347-58. [10.1159/000169122](#)
2. Visconti L, Cernaro V, Ricciardi CA, et al.: Renal biopsy: Still a landmark for the nephrologist. *World J Nephrol.* 2016, 5:321-7. [10.5527/wjn.v5.i4.321](#)
3. Bandari J, Fuller TW, Turner RM II, D'Agostino LA: Renal biopsy for medical renal disease: indications and contraindications. *Can J Urol.* 2016, 23:8121-6.
4. Gauthier BG, Mahadeo RS, Trachtman H: Techniques for percutaneous renal biopsies. *Pediatr Nephrol.* 1993, 7:457-63. [10.1007/BF00857575](#)
5. Uppot RN, Harisinghani MG, Gervais DA: Imaging-guided percutaneous renal biopsy: rationale and approach. *AJR Am J Roentgenol.* 2010, 194:1443-9. [10.2214/AJR.10.4427](#)
6. Fogo AB: Approach to renal biopsy. *Am J Kidney Dis.* 2003, 42:826-36. [10.1053/S0272-6386\(03\)01054-0](#)
7. Denic A, Lieske JC, Chakkera HA, et al.: The Substantial Loss of Nephrons in Healthy Human Kidneys with Aging. *J Am Soc Nephrol.* 2017, 28:313-20. [10.1681/ASN.2016020154](#)
8. Kremers WK, Denic A, Lieske JC, et al.: Distinguishing age-related from disease-related glomerulosclerosis on kidney biopsy: the Aging Kidney Anatomy study. *Nephrol Dial Transplant.* 2015, 30:2034-9. [10.1093/ndt/gfv072](#)
9. Glasscock RJ, Winearls C: Ageing and the Glomerular Filtration Rate: Truths and Consequences. *Trans Am Clin Climatol Assoc.* 2009, 120:419-28.
10. Ravizzini PI, Lino H, Fleury EF, Rangel DA, de Toledo LG: Comparative analysis of ultrasound-guided percutaneous biopsy of native kidneys in children and adults using the free-flank supine antero-lateral decubitus positioning. *Abdom Radiol (NY).* 2024, 49:1638-45. [10.1007/s00261-024-04316-6](#)
11. Gesualdo L, Cormio L, Stallone G, et al.: Percutaneous ultrasound-guided renal biopsy in supine antero-lateral position: a new approach for obese and non-obese patients. *Nephrol Dial Transplant.* 2008, 23:971-6. [10.1093/ndt/gfm669](#)

12. Torigoe K, Sakamoto R, Abe S, Muta K, Mukae H, Nishino T: Factors Associated with Glomerular Yield in Percutaneous Kidney Biopsy. *J Clin Med.* 2023, 12: [10.3390/jcm12123877](https://doi.org/10.3390/jcm12123877)
13. Zhan T, Lou A: Comparison of outcomes of an 18-gauge vs 16-gauge ultrasound-guided percutaneous renal biopsy: a systematic review and meta-analysis. *Ren Fail.* 2023, 45:2257806. [10.1080/0886022X.2023.2257806](https://doi.org/10.1080/0886022X.2023.2257806)
14. Schnuelle P: Renal Biopsy for Diagnosis in Kidney Disease: Indication, Technique, and Safety . *J Clin Med.* 2023, 12:[10.3390/jcm12196424](https://doi.org/10.3390/jcm12196424)
15. Helvacı Ö, Korucu B, Gonul İİ, Arınoy T, Guz G, Derici U: Kidney biopsy in the elderly: diagnostic adequacy and yield. *Int Urol Nephrol.* 2021, 53:105-9. [10.1007/s11255-020-02640-6](https://doi.org/10.1007/s11255-020-02640-6)

## **5. CONSIDERAÇÕES FINAIS**

Os resultados obtidos nesta linha de pesquisa sugerem que a biópsia renal percutânea guiada por ultrassonografia em posição supina ântero-lateral com flanco livre constitui técnica segura e eficaz para obtenção de tecido renal adequado para diagnóstico histopatológico. A técnica mostrou-se particularmente vantajosa na população pediátrica, onde o maior rendimento glomerular e as facilidades no manejo anestésico representam benefícios significativos em relação à abordagem convencional.

O gradiente etário observado no rendimento glomerular entre os subgrupos adultos reforça a importância de considerar as características individuais de cada paciente no planejamento do procedimento. Em pacientes idosos, estratégias como obtenção de maior número de fragmentos ou uso de agulhas com calibre ligeiramente maior podem ser necessárias para garantir diagnóstico adequado.

Os dois artigos científicos que sustentam esta tese, publicados em periódicos qualificados, juntos procuram oferecer contribuição para o avanço do conhecimento na área de nefrologia intervencionista, com implicações práticas diretas para a melhoria da qualidade assistencial oferecida aos pacientes.

Como perspectivas futuras, destacam-se a necessidade de estudos comparativos diretos entre as posições supino oblíqua ântero-lateral e prona, a avaliação de diferentes calibres de agulha em subgrupos etários específicos e a análise de custo-efetividade da técnica em diferentes contextos assistenciais. Estas pesquisas adicionais contribuirão para o refinamento contínuo das técnicas de biópsia renal, visando sempre a excelência diagnóstica com máxima segurança para os pacientes.

## 6. REFERÊNCIAS BIBLIOGRÁFICAS

1. Jha V, Garcia-Garcia G, Iseki K, et al. Chronic kidney disease: global dimension and perspectives. *Lancet*. 2013;382(9888):260-272. [https://doi.org/10.1016/S0140-6736\(13\)60687-X](https://doi.org/10.1016/S0140-6736(13)60687-X)
2. Webster AC, Nagler EV, Morton RL, Masson P. Chronic kidney disease. *Lancet*. 2017;389(10075):1238-1252. [https://doi.org/10.1016/S0140-6736\(16\)32064-5](https://doi.org/10.1016/S0140-6736(16)32064-5)
3. Levey AS, Coresh J. Chronic kidney disease. *Lancet*. 2012;379(9811):165-180. [https://doi.org/10.1016/S0140-6736\(11\)60178-5](https://doi.org/10.1016/S0140-6736(11)60178-5)
4. Glassock RJ, Warnock DG, Delanaye P. The global burden of chronic kidney disease: estimates, variability and pitfalls. *Nat Rev Nephrol*. 2017;13(2):104-114. <https://doi.org/10.1038/nrneph.2016.163>
5. Jennette JC, Falk RJ, Bacon PA, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum*. 2013;65(1):1-11. <https://doi.org/10.1002/art.37715>
6. Sesso RC, Lopes AA, Thomé FS, et al. Brazilian Dialysis Census: analysis of data from the 2009-2018 decade. *J Bras Nefrol*. 2020;42(2):191-200. <https://doi.org/10.1590/2175-8239-JBN-2019-0234>
7. Malafronte P, Mastroianni-Kirsztajn G, Betônico GN, et al. Paulista Registry of glomerulonephritis: 5-year data report. *Nephrol Dial Transplant*. 2006;21(11):3098-3105. <https://doi.org/10.1093/ndt/gfl237>
8. Rivera F, López-Gómez JM, Pérez-García R. Clinicopathologic correlations of renal pathology in Spain. *Kidney Int*. 2004;66(3):898-904. <https://doi.org/10.1111/j.1523-1755.2004.00831.x>
9. Wilhelmus S, Alpers CE, Cook HT, et al. The revisited classification of GN in SLE at 10 years: time to re-evaluate histopathologic lesions. *J Am Soc Nephrol*. 2015;26(12):2938-2946. <https://doi.org/10.1681/ASN.2015040384>
10. Trautmann A, Bodria M, Ozaltin F, et al. Spectrum of steroid-resistant and congenital nephrotic syndrome in children: the PodoNet registry cohort. *Clin J Am Soc Nephrol*. 2015;10(4):592-600. <https://doi.org/10.2215/CJN.06260614>
11. Iversen P, Brun C. Aspiration biopsy of the kidney. *Am J Med*. 1951;11(3):324-330. [https://doi.org/10.1016/0002-9343\(51\)90169-6](https://doi.org/10.1016/0002-9343(51)90169-6)

12. Corapi KM, Chen JL, Balk EM, Gordon CE. Bleeding complications of native kidney biopsy: a systematic review and meta-analysis. *Am J Kidney Dis*. 2012;60(1):62-73. <https://doi.org/10.1053/j.ajkd.2012.02.330>
13. Whittier WL, Korbet SM. Timing of complications in percutaneous renal biopsy. *J Am Soc Nephrol*. 2004;15(1):142-147. <https://doi.org/10.1097/01.ASN.0000102472.37947.14>
14. Hogan JJ, Mocanu M, Berns JS. The native kidney biopsy: update and evidence for best practice. *Clin J Am Soc Nephrol*. 2016;11(2):354-362. <https://doi.org/10.2215/CJN.05750515>
15. Poggio ED, McClelland RL, Blank KN, et al. Systematic review and meta-analysis of native kidney biopsy complications. *Clin J Am Soc Nephrol*. 2020;15(11):1595-1602. <https://doi.org/10.2215/CJN.04710420>
16. Maya ID, Maddela P, Barker J, Allon M. Percutaneous renal biopsy: comparison of blind and real-time ultrasound-guided technique. *Semin Dial*. 2007;20(4):355-358. <https://doi.org/10.1111/j.1525-139X.2007.00306.x>
17. Moutzouris DA, Herlitz L, Appel GB, et al. Renal biopsy in the very elderly. *Clin J Am Soc Nephrol*. 2009;4(6):1073-1082. <https://doi.org/10.2215/CJN.00990209>
18. Simard-Meilleur MC, Troyanov S, Roy L, et al. Risk factors and timing of native kidney biopsy complications. *Nephron Extra*. 2014;4(1):42-49. <https://doi.org/10.1159/000360691>
19. Tondel C, Vikse BE, Bostad L, Svarstad E. Safety and complications of percutaneous kidney biopsies in 715 children and 8573 adults in Norway 1988-2010. *Clin J Am Soc Nephrol*. 2012;7(10):1591-1597. <https://doi.org/10.2215/CJN.02150212>
20. Enríquez R, Martínez M, Amorós F, et al. Evaluation of the oblique supine position for percutaneous renal biopsy. *Nefrologia*. 2003;23(2):160-164.
21. Gesualdo L, Cormio L, Stallone G, et al. Percutaneous ultrasound-guided renal biopsy in supine antero-lateral position: a new approach for obese and non-obese patients. *Nephrol Dial Transplant*. 2008;23(3):971-976. <https://doi.org/10.1093/ndt/gfm669>
22. Santangelo L, Netti GS, Giordano P, et al. Indications and results of renal biopsy in children: a 36-year experience. *World J Pediatr*. 2018;14(2):127-133. <https://doi.org/10.1007/s12519-018-0147-5>

23. Pump B, Talleruphuus U, Christensen NJ, et al. Effects of supine, prone, and lateral positions on cardiovascular and renal variables in humans. *Am J Physiol Regul Integr Comp Physiol*. 2002;283(1):R174-R180. <https://doi.org/10.1152/ajpregu.00619.2001>
24. Uppot RN, Harisinghani MG, Gervais DA. Imaging-guided percutaneous renal biopsy: rationale and approach. *AJR Am J Roentgenol*. 2010;194(6):1443-1449. <https://doi.org/10.2214/AJR.10.4427>
25. Visconti L, Cernaro V, Ricciardi CA, et al. Renal biopsy: still a landmark for the nephrologist. *World J Nephrol*. 2016;5(4):321-327. <https://doi.org/10.5527/wjn.v5.i4.321>
26. Gesualdo L, Di Palma AM, Morrone LF, et al. The Italian experience of the national registry of renal biopsies. *Kidney Int*. 2004;66(3):890-894. <https://doi.org/10.1111/j.1523-1755.2004.00830.x>
27. Bandari J, Fuller TW, Turner RM, D'Agostino LA. Renal biopsy for medical renal disease: indications and contraindications. *Can J Urol*. 2016;23(5):8121-8126.
28. Mantan M, Batra V. Renal biopsy in children. *Indian Pediatr*. 2020;57(5):452-458. <https://doi.org/10.1007/s13312-020-1818-6>
29. Franke M, Kramarczyk A, Taylan C, et al. Ultrasound-guided percutaneous renal biopsy in 295 children and adolescents: role of ultrasound and analysis of complications. *PLoS One*. 2014;9(12):e114737. <https://doi.org/10.1371/journal.pone.0114737>
30. Feneberg R, Schaefer F, Zieger B, et al. Percutaneous renal biopsy in children: a 27-year experience. *Nephron*. 1998;79(4):438-446. <https://doi.org/10.1159/000045090>
31. Walker PD. The renal biopsy. *Arch Pathol Lab Med*. 2009;133(2):181-188. <https://doi.org/10.5858/133.2.181>
32. Korbet SM. Percutaneous renal biopsy. *Semin Nephrol*. 2002;22(3):254-267. <https://doi.org/10.1053/snep.2002.31712>
33. Kheda MF, Brenner RM, Patel MN, et al. Influence of patient selection on percutaneous renal biopsy outcomes. *Clin Nephrol*. 2013;79(6):417-425. <https://doi.org/10.5414/CN107655>
34. Chen TK, Estrella MM, Fine DM. Predictors of kidney biopsy complication among patients with systemic lupus erythematosus. *Lupus*. 2012;21(8):848-854. <https://doi.org/10.1177/0961203312437809>

35. Prasad N, Kumar S, Manjunath R, et al. Real-time ultrasound-guided percutaneous renal biopsy with needle guide by nephrologists decreases post-biopsy complications. *Clin Kidney J*. 2015;8(2):151-156. <https://doi.org/10.1093/ckj/sfv012>
36. Denic A, Lieske JC, Chakkera HA, et al. The substantial loss of nephrons in healthy human kidneys with aging. *J Am Soc Nephrol*. 2017;28(2):313-320. <https://doi.org/10.1681/ASN.2016020154>
37. Cameron JS, Hicks J: The introduction of renal biopsy into nephrology from 1901 to 1961: a paradigm of the forming of nephrology by technology. *Am J Nephrol*. 1997, 17:347-58. 10.1159/000169122
38. Bandari J, Fuller TW, Turner RM II, D'Agostino LA: Renal biopsy for medical renal disease: indications and contraindications. *Can J Urol*. 2016, 23:8121-6.
39. Gauthier BG, Mahadeo RS, Trachtman H: Techniques for percutaneous renal biopsies. *Pediatr Nephrol*.1993, 7:457-63. 10.1007/BF00857575
40. Uppot RN, Harisinghani MG, Gervais DA: Imaging-guided percutaneous renal biopsy: rationale and approach. *AJR Am J Roentgenol*. 2010, 194:1443-9. 10.2214/AJR.10.4427
41. Fogo AB: Approach to renal biopsy. *Am J Kidney Dis*. 2003, 42:826-36. 10.1053/S0272-6386(03)01054-0
42. Denic A, Lieske JC, Chakkera HA, et al.: The Substantial Loss of Nephrons in Healthy Human Kidneys with Aging. *J Am Soc Nephrol*. 2017, 28:313-20. 10.1681/ASN.2016020154
43. Kremers WK, Denic A, Lieske JC, et al.: Distinguishing age-related from disease-related glomerulosclerosis on kidney biopsy: the Aging Kidney Anatomy study. *Nephrol Dial Transplant*. 2015, 30:2034-9.10.1093/ndt/gfv072
44. Ravizzini PI, Lino H, Fleury EF, Rangel DA, de Toledo LG: Comparative analysis of ultrasound-guided percutaneous biopsy of native kidneys in children and adults using the free-flank supine antero-lateral decubitus positioning. *Abdom Radiol (NY)*. 2024, 49:1638-45. 10.1007/s00261-024-04316-6
45. Torigoe K, Sakamoto R, Abe S, Muta K, Mukae H, Nishino T: Factors Associated with Glomerular Yield in Percutaneous Kidney Biopsy. *J Clin Med*. 2023, 12: 10.3390/jcm12123877

46. Zhan T, Lou A: Comparison of outcomes of an 18-gauge vs 16-gauge ultrasound-guided percutaneous renal biopsy: a systematic review and meta-analysis. *Ren Fail.* 2023, 45:2257806.  
10.1080/0886022X.2023.2257806
47. Schnuelle P: Renal Biopsy for Diagnosis in Kidney Disease: Indication, Technique, and Safety . *J Clin Med.* 2023, 12:10.3390/jcm12196424
48. Helvacı Ö, Korucu B, Gonul İİ, Arınsoy T, Guz G, Derici U: Kidney biopsy in the elderly: diagnostic adequacy and yield. *Int Urol Nephrol.* 2021, 53:105-9. 10.1007/s11255-020-02640-6 2025

**7. ANEXOS**

**7.1. Parecer Comitê de Ética em Pesquisa em Seres Humanos da Santa Casa de São Paulo**



SANTA CASA DE  
MISERICÓRDIA DE SÃO



**PARECER CONSUBSTANCIADO DO CEP**

**DADOS DO PROJETO DE PESQUISA**

**Título da Pesquisa:** Análise comparativa da taxa de sucesso e complicações em biópsias orientadas por ultrassonografia de rins nativos em decúbito supino anterolateral com flanco livre na população pediátrica e adulta

**Pesquisador:** Pedro Ravizzini

**Área Temática:**

**Versão:** 2

**CAAE:** 48707221.4.0000.5479

**Instituição Proponente:** INCT-HPV/Faculdade de Ciências Médicas Santa Casa de Misericórdia de

**Patrocinador Principal:** Financiamento Próprio

**DADOS DO PARECER**

**Número do Parecer:** 5.122.737

**Apresentação do Projeto:**

Análise comparativa da taxa de sucesso e complicações em biópsias orientadas por ultrassonografia de rins nativos em decúbito supino anterolateral com flanco livre na população pediátrica e adulta

Pedro Ravizzini

Mestrado

**Objetivo da Pesquisa:**

Comparar as taxas de sucesso e complicações em biópsias renais orientadas por ultrassonografia em decúbito supino anterolateral em pacientes com até 15 anos de idade, definido como população pediátrica, e com mais de 15 anos de idade, definido como população adulta.

Objetivos específicos

Análise da prevalência de resultados positivos para as amostras.

Análise da prevalência de amostras com mais de 9 glomérulos.

Análise da prevalência de intercorrências.

Análise de razão de prevalência / odds ratio e análise por regressão linear para avaliação da relação entre taxas de sucesso e faixa etária, aferida pela obtenção de amostra superior a 9 glomérulos ou obtenção de amostra suficiente para diagnóstico histológico.

Análise da taxa de complicações comparada entre as populações adulta e pediátrica.

**Endereço:** Rua Marques de Itu, 381

**Bairro:** VILA BUARQUE

**CEP:** 01.223-001

**UF:** SP

**Município:** SAO PAULO

**Telefone:** (11)2176-1817

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## SANTA CASA DE MISERICÓRDIA DE SÃO



Continuação do Parecer: 5.122.737

Análise da interferência de fatores secundários, como altura, peso, índice de massa corpórea (IMC), tipo de anestesia e lateralidade da amostra em relação às taxas de sucesso e complicação do procedimento.

### **Avaliação dos Riscos e Benefícios:**

Estudo retrospectivo, análise de prontuários, além da quebra de confidencialidade, não oferece riscos.

Benefícios relacionados à construção do conhecimento sobre o assunto.

### **Comentários e Considerações sobre a Pesquisa:**

Clara e objetiva.

### **Considerações sobre os Termos de apresentação obrigatória:**

Adequados.

### **Recomendações:**

Sem recomendações.

### **Conclusões ou Pendências e Lista de Inadequações:**

Sem pendências.

### **Considerações Finais a critério do CEP:**

**Este parecer foi elaborado baseado nos documentos abaixo relacionados:**

| Tipo Documento                                   | Arquivo                                       | Postagem            | Autor                  | Situação |
|--------------------------------------------------|-----------------------------------------------|---------------------|------------------------|----------|
| Informações Básicas do Projeto                   | PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_1775646.pdf | 22/11/2021 11:43:52 |                        | Aceito   |
| Projeto Detalhado / Brochura Investigador        | PROJETO_DE_PESQUISA.docx                      | 02/11/2021 13:09:41 | Pedro Ravizzini        | Aceito   |
| Declaração de Instituição e Infraestrutura       | Of_ACPC_02112021.pdf                          | 30/06/2021 15:00:25 | HAMANDA SILVA OLIVEIRA | Aceito   |
| Outros                                           | AUTORIZACAO.pdf                               | 28/06/2021 15:01:26 | Pedro Ravizzini        | Aceito   |
| Outros                                           | COMPROMISSO_RELATORIOS.pdf                    | 25/06/2021 10:34:48 | Pedro Ravizzini        | Aceito   |
| TCLE / Termos de Assentimento / Justificativa de | TCLE_DISPENSA.pdf                             | 25/06/2021 10:33:20 | Pedro Ravizzini        | Aceito   |

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## SANTA CASA DE MISERICÓRDIA DE SÃO



Continuação do Parecer: 5.122.737

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|----------------|--------------------------|------------------------|-----------------|--------|
| Ausência       | TCLE_DISPENSA.pdf        | 25/06/2021<br>10:33:20 | Pedro Ravizzini | Aceito |
| Cronograma     | CRONOGRAMA.pdf           | 25/06/2021<br>10:33:09 | Pedro Ravizzini | Aceito |
| Orçamento      | ORCAMENTO.pdf            | 25/06/2021<br>10:31:59 | Pedro Ravizzini | Aceito |
| Outros         | COMPROMISSO_SDI.pdf      | 23/06/2021<br>19:25:47 | Pedro Ravizzini | Aceito |
| Outros         | COMISSAO_INTERNA_SDI.pdf | 23/06/2021<br>19:25:26 | Pedro Ravizzini | Aceito |
| Folha de Rosto | FOLHA_DE_ROSTO.pdf       | 23/06/2021<br>19:22:52 | Pedro Ravizzini | Aceito |

**Situação do Parecer:**

Aprovado

**Necessita Apreciação da CONEP:**

Não

SAO PAULO, 24 de Novembro de 2021

---

**Assinado por:**  
**Rosane Lowenthal**  
**(Coordenador(a))**

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## 7.2. Normas de submissão da Revista *Abdominal Radiology*

### Submission guidelines

#### Instructions for Authors

##### Important Information on Manuscript Preparation and Submission

This journal recently switched to a different submission and peer review system. In order to ensure that the author(s) remain anonymous to the reviewers throughout the peer review process, you will be asked to submit certain information and statements directly in the system's interface instead of including it in the manuscript or on a separate title page. We are currently working on revising our submission guidelines to reflect this properly. When preparing your manuscript, please make sure to have all the necessary author details and statements as described below at hand, but please note that you will have to submit some of them via the according fields in the system's interface during submission and not on a separate title page.

##### SNAPP Double Anonymous Peer Review Guidelines

##### Important Notice for Submissions to Special Collections

We are delighted by the interest shown in our special collections. To maintain the high standards and relevance of these collections, please be advised of the following guidelines for submissions:

##### Submission Guidelines for Special Collections:

1. **Invited Submissions:** Most articles included in our special collections are by invitation from guest editors. If you have not been invited by a guest editor, please ensure that your manuscript aligns closely with the scope and objectives of the collection.
2. **Relevance:** Before submitting, carefully review the specific aims and topics covered by the collection to ensure that your work is relevant.
3. **Initial Review:** Submissions that do not meet the scope of the collection may be returned without review. To avoid this, please ensure your submission is pertinent and well-suited to the collection's focus.
4. **Contact for Queries:** If you are unsure whether your manuscript is suitable for a particular collection, please contact the guest editor or editor-in-chief for clarification before submitting.

These measures are designed to streamline the submission process and ensure that all contributions to our special collections meet the intended standards and scope.

##### General Information

Please note that the journal does not offer pre-evaluation. Therefore please directly submit your manuscript and the Editor will then contact you.

It is the Corresponding Author's responsibility to ensure that he/she has the correct authors' names, affiliations, addresses and author sequence when the final corrected proofs are submitted. Please keep in mind that corrections are no longer possible after online first publication. All additional corrections after publication need the approval of the Editor-in-Chief(s) and would result in the publication of an erratum that will be hyperlinked to the article.

Articles are checked for duplication. Articles with duplications considered excessive will not be published. If data from another publication is included, this should be clearly stated in the manuscript and referenced. In addition, how the submitted work differs from prior publications should be specifically stated.

Do not include reference to the authors name or institution within the manuscript.

The use of abbreviations and acronyms is highly discouraged, as it makes reading a paper difficult if those abbreviations are not familiar. Only widely understood abbreviations or acronyms should be used.

Please include the key take home message in the last sentence or paragraph of both the abstract and the discussion.

Figures should be included to illustrate the major findings of the study. Excessive figures should be avoided. Each figure should include a legend and pertinent arrows to the findings. Pictorial essays and reviews should be image-rich, but focused on major teaching points. An atlas of images that includes minor or uncommon imaging findings is discouraged.

Tables can be included if they present a more understandable means of explaining findings than data included in text. Tables should be condensed so that key findings are demonstrated. The table data should not be duplicated within the text. A record of all the study data in a table is generally not useful to readers and is discouraged.

##### Types of papers

##### Research/Meta-analysis

- Word Count: Maximum 3500 words.
- Abstract: Structured, 300 words, covering objectives, methods, results, and conclusion.
- Figures: Maximum of 5 (A figure may consist of multiple images)
- Images: Maximum of 10
- Tables: Maximum of 5
- References: Up to 60.

- Please submit Meta-analysis as "Review".

#### **Review**

- Word Count: Maximum 4500 words.
- Abstract: Unstructured, less than 300 words.
- Figures: Maximum of 6 (A figure may consist of multiple images)
- Images: Maximum of 15
- Tables: Maximum of 3
- References: Up to 60.

#### **Pictorial Essay (submit as Review)**

- Word Count: Maximum 2500 words.
- Abstract: Unstructured, less than 200 words.
- Figures: Maximum of 8 (A figure may consist of multiple images)
- Images: Maximum of 20
- Tables: Maximum of 3
- References: Up to 30.

#### **Perspective**

- Word Count: Maximum 3500 words.
- Abstract: Not required but an unstructured abstract of less than 300 words can be included.
- Figures/Tables: Up to 3.
- References: Up to 25.

#### **Classics in Abdominal Radiology (submit as Image)**

- Word Count: Maximum 1500 words.
- Abstract: Not required but an unstructured abstract of less than 100 words can be included.
- Figures/Tables: Up to 5.
- References: Up to 15.

#### **Perspective from SAR (submit as Perspective)**

- Word Count: Maximum 3000 words.
- Abstract: Unstructured, less than 300 words.
- Figures/Tables: Up to 5.
- References: Up to 30, focusing on policy, guidelines, or consensus statements.

#### **Society Report (submit as Correspondence)**

- Word Count: Maximum 3500 words.
- Abstract: Unstructured, less than 300 words.
- Figures/Tables: Up to 5.
- References: Up to 30, focusing on society activities, milestones, or future directions.

#### **Matters Arising/Comment**

- Word Count: Maximum 1000 words.
- Abstract: Not required
- Figures/Tables: Up to 2 (only if necessary).
- References: Up to 10.
- Please note: Commentaries are invited only.

#### **Double-blind peer review**

This journal follows a double-blind reviewing procedure. This means that the author will remain anonymous to the reviewers throughout peer review. It is the responsibility of the author to anonymize the manuscript and any associated materials.

- Author names, affiliations and any other potentially identifying information should be removed from the manuscript text and any accompanying files (such as figures of supplementary material);
- A separate Title Page should be submitted, containing title, author names, affiliations, and the contact information of the corresponding author. Any acknowledgements, disclosures, or funding information should also be included on this page;
- Authors should avoid citing their own work in a way that could reveal their identity.

#### **Manuscript Submission**

Submission of a manuscript implies: that the work described has not been published before; that it is not under consideration for publication anywhere else; that its publication has been approved by all co-authors, if any, as well as by the responsible authorities – tacitly or explicitly – at the institute where the work has been carried out. The publisher will not be held legally responsible should there be any claims for compensation.

#### **Permissions**

Authors wishing to include figures, tables, or text passages that have already been published elsewhere are required to obtain permission from the copyright owner(s) for both the print and online format and to include evidence that such permission has been granted when submitting their papers. Any material received without such evidence will be assumed to originate from the authors.

#### **Online Submission**

Please follow the hyperlink "Submit manuscript" and upload all of your manuscript files following the instructions given on the screen.

#### **Source Files**

Please ensure you provide all relevant editable source files at every submission and revision. Failing to submit a complete set of editable source files will result in your article not being considered for review. For your manuscript text please always submit in common word processing formats such as .docx or LaTeX.

#### **Submitting Declarations**

Please note that Author Contribution information and Competing Interest information must be provided at submission via the submission interface. Only the information submitted via the interface will be used in the final published version. Please make sure that if you are an editorial board member and also a listed author that you also declare this information in the Competing Interest section of the interface.

Please see the relevant sections in the submission guidelines for further information on these statements as well as possible other mandatory statements.

#### **Title Page**

Please make sure your title page contains the following information.

##### **Title**

The title should be concise and informative.

##### **Author information**

- The name(s) of the author(s)
- The affiliation(s) of the author(s), i.e. institution, (department), city, (state), country
- A clear indication and an active e-mail address of the corresponding author
- If available, the 16-digit ORCID of the author(s)

If address information is provided with the affiliation(s) it will also be published.

For authors that are (temporarily) unaffiliated we will only capture their city and country of residence, not their e-mail address unless specifically requested.

Large Language Models (LLMs), such as ChatGPT, do not currently satisfy our authorship criteria. Notably an attribution of authorship carries with it accountability for the work, which cannot be effectively applied to LLMs. Use of an LLM should be properly documented in the Methods section (and if a Methods section is not available, in a suitable alternative part) of the manuscript. The use of an LLM (or other AI-tool) for "AI assisted copy editing" purposes does not need to be declared. In this context, we define the term "AI assisted copy editing" as AI-assisted improvements to human-generated texts for readability and style, and to ensure that the texts are free of errors in grammar, spelling, punctuation and tone. These AI-assisted improvements may include wording and formatting changes to the texts, but do not include generative editorial work and autonomous content creation. In all cases, there must be human accountability for the final version of the text and agreement from the authors that the edits reflect their original work.

#### **Abstract**

Please provide a structured abstract of 150 to 250 words which should be divided into the following sections:

- Purpose (stating the main purposes and research question)
- Methods
- Results
- Conclusion

*For life science journals only (when applicable)*

- Trial registration number and date of registration for prospectively registered trials
- Trial registration number and date of registration followed by "retrospectively registered", for retrospectively registered trials

#### **Keywords**

Please provide 4 to 6 keywords which can be used for indexing purposes.

#### **Statements and Declarations**

The following statements should be included under the heading "Statements and Declarations" for inclusion in the published paper. Please note that submissions that do not include relevant declarations will be returned as incomplete.

- **Competing Interests:** Authors are required to disclose financial or non-financial interests that are directly or indirectly related to the work submitted for publication. Please refer to "Competing Interests and Funding" below for more information on how to complete this section.

Please see the relevant sections in the submission guidelines for further information as well as various examples of wording. Please revise/customize the sample statements according to your own needs.

The U.S. National Library of Medicine (NLM) provides a curated medical vocabulary resource: Medical Subject Headings (MeSH). Please ensure that your keywords can be found within the MeSH by searching your keywords on <https://meshb.nlm.nih.gov/search>. In order to find suitable keywords from your abstract the MeSH on Demand tool might be helpful: <https://meshb.nlm.nih.gov/MeSHonDemand>.

#### **Specific Remark**

- Any acknowledgements, disclosures or funding information should only be stated on the Title page, not in the main body of the manuscript.

#### **Text Formatting**

Manuscripts should be submitted in Word.

- Use a normal, plain font (e.g., 10-point Times Roman) for text.
- Use italics for emphasis.
- Use the automatic page numbering function to number the pages.
- Do not use field functions.
- Use tab stops or other commands for indents, not the space bar.
- Use the table function, not spreadsheets, to make tables.
- Use the equation editor or MathType for equations.
- Save your file in docx format (Word 2007 or higher) or doc format (older Word versions).

Manuscripts with mathematical content can also be submitted in LaTeX. We recommend using Springer Nature's LaTeX template.

#### **Headings**

Please use no more than three levels of displayed headings.

#### **Abbreviations**

Abbreviations should be defined at first mention and used consistently thereafter.

#### **Footnotes**

Footnotes can be used to give additional information, which may include the citation of a reference included in the reference list. They should not consist solely of a reference citation, and they should never include the bibliographic details of a reference. They should also not contain any figures or tables.

Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data). Footnotes to the title or the authors of the article are not given reference symbols.

Always use footnotes instead of endnotes.

#### **Acknowledgments**

Acknowledgments of people, grants, funds, etc. should be placed in a separate section on the title page. The names of funding organizations should be written in full.

#### **Scientific style**

Generic names of drugs and pesticides are preferred; if trade names are used, the generic name should be given at first mention.

#### **References**

##### **Citation**

Reference citations in the text should be identified by numbers in square brackets. Some examples:

1. Negotiation research spans many disciplines [3].
2. This result was later contradicted by Becker and Seligman [5].
3. This effect has been widely studied [1-3, 7].

##### **Reference list**

The list of references should only include works that are cited in the text and that have been published or accepted for publication. Personal communications and unpublished works should only be mentioned in the text.

The entries in the list should be numbered consecutively.

If available, please always include DOIs as full DOI links in your reference list (e.g. "https://doi.org/abc").

- Journal article

Gamelin FX, Baquet G, Berthoin S, Thevenet D, Nourry C, Nottin S, Bosquet L (2009) Effect of high intensity intermittent training on heart rate variability in prepubescent children. *Eur J Appl Physiol* 105:731-738. <https://doi.org/10.1007/s00421-008-0955-8>

Ideally, the names of all authors should be provided, but the usage of "et al" in long author lists will also be accepted:

Smith J, Jones M Jr, Houghton L et al (1999) Future of health insurance. *N Engl J Med* 965:325–329

- Article by DOI

Slifka MK, Whitton JL (2000) Clinical implications of dysregulated cytokine production. *J Mol Med*. <https://doi.org/10.1007/s001090000086>

- Book

South J, Blass B (2001) *The future of modern genomics*. Blackwell, London

- Book chapter  
Brown B, Aaron M (2001) The politics of nature. In: Smith J (ed) The rise of modern genomics, 3rd edn. Wiley, New York, pp 230-257
  - Online document  
Cartwright J (2007) Big stars have weather too. IOP Publishing PhysicsWeb. <http://physicsweb.org/articles/news/11/6/16/1>. Accessed 26 June 2007
  - Dissertation  
Trent JW (1975) Experimental acute renal failure. Dissertation, University of California
- Always use the standard abbreviation of a journal's name according to the ISSN List of Title Word Abbreviations, see ISSN.org LTWA
- If you are unsure, please use the full journal title.
- Authors preparing their manuscript in LaTeX can use the bibliography style file sn-basic.bst which is included in the Springer Nature Article Template.

### Tables

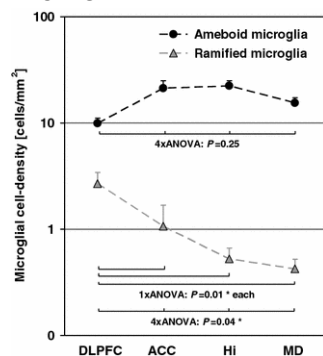
- All tables are to be numbered using Arabic numerals.
- Tables should always be cited in text in consecutive numerical order.
- For each table, please supply a table caption (title) explaining the components of the table.
- Identify any previously published material by giving the original source in the form of a reference at the end of the table caption.
- Footnotes to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data) and included beneath the table body.

### Artwork and Illustrations Guidelines

#### Electronic Figure Submission

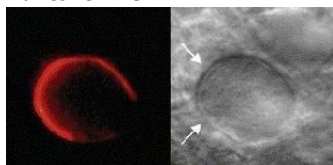
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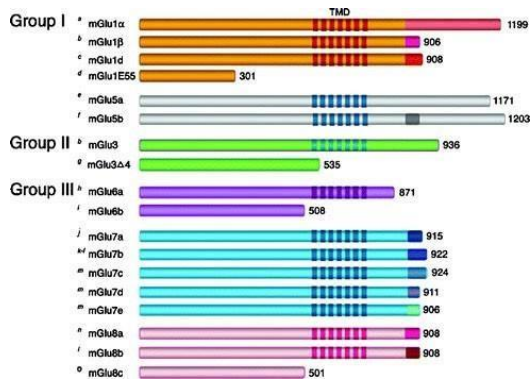
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Research Resource Identifiers (RRID) are persistent unique identifiers (effectively similar to a DOI) for research resources. This journal encourages authors to adopt RRIDs when reporting key biological resources (antibodies, cell lines, model organisms and tools) in their manuscripts.

#### **Clinical Trial Registration**

The World Health Organization (WHO) definition of a clinical trial is "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes". The WHO defines health interventions as "A health intervention is an act performed for, with or on behalf of a person or population whose purpose is to assess, improve, maintain, promote or

modify health, functioning or health conditions” and a health-related outcome is generally defined as a change in the health of a person or population as a result of an intervention.

To ensure the integrity of the reporting of patient-centered trials, authors must register prospective clinical trials (phase II to IV trials) in suitable publicly available repositories. For example [www.clinicaltrials.gov](http://www.clinicaltrials.gov) or any of the primary registries that participate in the WHO International Clinical Trials Registry Platform.

The trial registration number (TRN) and date of registration should be included as the last line of the manuscript abstract.

For clinical trials that have not been registered prospectively, authors are encouraged to register retrospectively to ensure the complete publication of all results. The trial registration number (TRN), date of registration and the words ‘retrospectively registered’ should be included as the last line of the manuscript abstract.

### **Standards of reporting**

Springer Nature advocates complete and transparent reporting of biomedical and biological research and research with biological applications. Authors are recommended to adhere to the minimum reporting guidelines hosted by the [EQUATOR Network](#) when preparing their manuscript.

### **Summary of requirements**

The above should be summarized in a statement and placed in a ‘Declarations’ section before the reference list under a heading of ‘Ethics approval’.

Examples of statements to be used when ethics approval has been obtained:

- All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Bioethics Committee of the Medical University of A (No ).
- This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of University B (Date.../No ).
- Approval was obtained from the ethics committee of University C. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.
- The questionnaire and methodology for this study was approved by the Human Research Ethics committee of the University of D (Ethics approval number ).

Examples of statements to be used for a retrospective study:

- Ethical approval was waived by the local Ethics Committee of University A in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.
- This research study was conducted retrospectively from data obtained for clinical purposes. We consulted extensively with the IRB of XYZ who determined that our study did not need ethical approval. An IRB official waiver of ethical approval was granted from the IRB of XYZ.
- This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Human Investigation Committee (IRB) of University B approved this study.

Examples of statements to be used when no ethical approval is required/exemption granted:

- This is an observational study. The XYZ Research Ethics Committee has confirmed that no ethical approval is required.
- The data reproduced from Article X utilized human tissue that was procured via our Biobank AB, which provides de-identified samples. This study was reviewed and deemed exempt by our XYZ Institutional Review Board. The BioBank protocols are in accordance with the ethical standards of our institution and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Authors are responsible for correctness of the statements provided in the manuscript. See also Authorship Principles. The Editor-in-Chief reserves the right to reject submissions that do not meet the guidelines described in this section.

### **Informed consent**

All individuals have individual rights that are not to be infringed. Individual participants in studies have, for example, the right to decide what happens to the (identifiable) personal data gathered, to what they have said during a study or an interview, as well as to any photograph that was taken. This is especially true concerning images of vulnerable people (e.g. minors, patients, refugees, etc) or the use of images in sensitive contexts. In many instances authors will need to secure written consent before including images.

Identifying details (names, dates of birth, identity numbers, biometrical characteristics (such as facial features, fingerprint, writing style, voice pattern, DNA or other distinguishing characteristic) and other information) of the participants that were studied should not be published in written descriptions, photographs, and genetic profiles unless the information is essential for scholarly purposes and the participant (or parent/guardian if the participant is a minor or incapable or legal representative) gave written informed consent for publication. Complete anonymity is difficult to achieve in some cases. Detailed descriptions of individual participants, whether of their whole bodies or of body sections, may lead to disclosure of their identity. Under certain circumstances consent is not required as long as information is anonymized and the submission does not include images that may identify the person.

Informed consent for publication should be obtained if there is any doubt. For example, masking the eye region in photographs of participants is inadequate protection of anonymity. If identifying characteristics are altered to protect anonymity, such as in genetic profiles, authors should provide assurance that alterations do not distort meaning.

Exceptions where it is not necessary to obtain consent:

- Images such as x rays, laparoscopic images, ultrasound images, brain scans, pathology slides unless there is a concern about identifying information in which case, authors should ensure that consent is obtained.
- Reuse of images: If images are being reused from prior publications, the Publisher will assume that the prior publication obtained the relevant information regarding consent. Authors should provide the appropriate attribution for republished images.

#### **Consent and already available data and/or biologic material**

Regardless of whether material is collected from living or dead patients, they (family or guardian if the deceased has not made a pre-mortem decision) must have given prior written consent. The aspect of confidentiality as well as any wishes from the deceased should be respected.

#### **Data protection, confidentiality and privacy**

When biological material is donated for or data is generated as part of a research project authors should ensure, as part of the informed consent procedure, that the participants are made aware what kind of (personal) data will be processed, how it will be used and for what purpose. In case of data acquired via a biobank/biorepository, it is possible they apply a broad consent which allows research participants to consent to a broad range of uses of their data and samples which is regarded by research ethics committees as specific enough to be considered "informed". However, authors should always check the specific biobank/biorepository policies or any other type of data provider policies (in case of non-bio research) to be sure that this is the case.

#### **Consent to Participate**

For all research involving human subjects, freely-given, informed consent to participate in the study must be obtained from participants (or their parent or legal guardian in the case of children under 16) and a statement to this effect should appear in the manuscript. In the case of articles describing human transplantation studies, authors must include a statement declaring that no organs/tissues were obtained from prisoners and must also name the institution(s)/clinic(s)/department(s) via which organs/tissues were obtained. For manuscripts reporting studies involving vulnerable groups where there is the potential for coercion or where consent may not have been fully informed, extra care will be taken by the editor and may be referred to the Springer Nature Research Integrity Group.

#### **Consent to Publish**

Individuals may consent to participate in a study, but object to having their data published in a journal article. Authors should make sure to also seek consent from individuals to publish their data prior to submitting their paper to a journal. This is in particular applicable to case studies. A consent to publish form can be found

#### **Summary of requirements**

The above should be summarized in a statement and placed in a 'Declarations' section before the reference list under a heading of 'Consent to participate' and/or 'Consent to publish'. Other declarations include Funding, Competing interests, Ethics approval, Consent, Data and/or Code availability and Authors' contribution statements.

Please see the various examples of wording below and revise/customize the sample statements according to your own needs.

#### **Sample statements for "Consent to participate":**

Informed consent was obtained from all individual participants included in the study.

Informed consent was obtained from legal guardians.

Written informed consent was obtained from the parents.

Verbal informed consent was obtained prior to the interview.

#### **Sample statements for "Consent to publish":**

The authors affirm that human research participants provided informed consent for publication of the images in Figure(s) 1a, 1b and 1c.

The participant has consented to the submission of the case report to the journal.

Patients signed informed consent regarding publishing their data and photographs.

Sample statements if identifying information about participants is available in the article:

Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

Authors are responsible for correctness of the statements provided in the manuscript. See also Authorship Principles. The Editor-in-Chief reserves the right to reject submissions that do not meet the guidelines described in this section.

Images will be removed from publication if authors have not obtained informed consent or the paper may be removed and replaced with a notice explaining the reason for removal.

#### **After acceptance**

Upon acceptance, your article will be exported to Production to undergo typesetting. Shortly after this you will receive two e-mails. One contains a request to confirm your affiliation, choose the publishing model for your

article, as well as to arrange rights and payment of any associated publication cost. A second e-mail containing a link to your article's proofs will be sent once typesetting is completed.

#### **Article publishing agreement**

Depending on the ownership of the journal and its policies, you will either grant the Publisher an exclusive licence to publish the article or will be asked to transfer copyright of the article to the Publisher.

#### **Offprints**

Offprints can be ordered by the corresponding author.

#### **Color illustrations**

Online publication of color illustrations is free of charge. For color in the print version, authors will be expected to make a contribution towards the extra costs.

#### **Proof reading**

The purpose of the proof is to check for typesetting or conversion errors and the completeness and accuracy of the text, tables and figures. Substantial changes in content, e.g., new results, corrected values, title and authorship, are not allowed without the approval of the Editor.

After online publication, further changes can only be made in the form of an Erratum, which will be hyperlinked to the article.

#### **Online First**

The article will be published online after receipt of the corrected proofs. This is the official first publication citable with the DOI. After release of the printed version, the paper can also be cited by issue and page numbers.

#### **Open Choice**

Open Choice allows you to publish open access in more than 1850 Springer Nature journals, making your research more visible and accessible immediately on publication.

Benefits:

- Increased researcher engagement: Open Choice enables access by anyone with an internet connection, immediately on publication.
- Higher visibility and impact: In Springer hybrid journals, OA articles are accessed 4 times more often on average, and cited 1.7 more times on average\*.
- Easy compliance with funder and institutional mandates: Many funders require open access publishing, and some take compliance into account when assessing future grant applications.

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\*) Within the first three years of publication. Springer Nature hybrid journal OA impact analysis, 2018.

#### **Copyright**

Open Choice articles do not require transfer of copyright as the copyright remains with the author. In opting for open access, the author(s) agree to publish the article under a Creative Commons license. Details of the OA licences offered to authors can be found on the individual journal page.

### 7.3. Normas de submissão da Revista CUREUS

#### Submitting an Article

Cureus operates a merit-based [publication system](#) in which we publish all articles that follow our submission guidelines and contain no fraudulent or dangerous science. It is the submitting author's responsibility to meet us halfway by submitting a draft of their medical research article that meets all listed editorial requirements.

Authors must complete the following steps to submit an article draft for peer review. Authors may save and exit the submission process at any time by clicking 'Exit' in the top right corner of the page.

#### Getting started

Are you submitting through one of our Cureus Channels? Are you entering a competition? Designate your article as a channel or competition article here, then choose the article type (original, review, case report, technical report, editorial). This information cannot be changed after moving on to the Title, etc. section of the [Cureus submission](#) process.

**Do not enter the title in all caps or include a period at the end.**

**Acronyms, initialisms or abbreviations are not permitted in the article title. Exceptions include common abbreviations such as COVID-1G, HIV, MRI, etc.**

Beginning with this step, you may preview your draft at any time to see how the published version will be displayed.

**Abstract:** 3500 characters limit

Abstract subheaders are permitted in original articles only.

**Keywords:** 5-10 keywords. Please keep your keywords short (a maximum of 3-4 words each) and as specific as possible.

#### Authors

Include all Authors. Add your co-authors. Authors cannot be added after submission, so make sure to include all [authors](#) before submitting your article! The submitting author is listed as the first author by default; this can be changed by dragging and dropping the authors into the desired order.

#### Check Author Names and Affiliations

While your co-authors can edit their name and affiliation in their Cureus profiles, their changes will not be reflected in article submissions or published articles in Cureus. Author names and affiliations for all authors listed in an article must be edited by the submitting author.

It is the submitting author's responsibility to enter or revise all co-author name and affiliation information to ensure accuracy, consistent formatting, and compliance with these article submission guidelines.

#### Affiliation Consistency Required

All authors must have an accurate and consistently formatted affiliation name and location. Medical students should list 'Medical School' or the relevant article category as their department during submission (e.g. neurosurgery, family medicine, etc.).

Titles such as Professor, Assistant Professor, Medical Student, Resident, Department Chair, etc. are not permitted in the author affiliation and should not be included in the Department field.

If two or more authors are from the same hospital or academic institution, the hospital or institution name entered in this field must be identical for those authors. If these authors are also from the same department, then the information in the department field must also be identical. This includes spelling, capitalization, spacing, etc.

Article submissions with inconsistent affiliation formatting will require the purchase of our [Preferred Editing](#) service to proceed, so this step is very important.

#### No Suffixes for Seniority in Author List

Suffixes denoting author list seniority or professional standing (e.g., Senior, Junior, II, III) should not be included in your Cureus submission.

#### Contributions

All authors must meet [ICMJE guidelines](#) for authorship to be listed as an author. Open the dropdown menu next to each author to select their contributions to the work.

Authors who do not satisfy ICMJE authorship criteria should be removed from the author list during article submission and mentioned in the Acknowledgements section (consent needed).

#### Disclosures

Please provide all relevant information about human or animal subjects and disclose relevant conflicts of interest (COI). You may also add acknowledgments at this time.

If human or animal subjects are included in the article, please provide the relevant IRB names and approval numbers and confirm that informed consent was obtained or waived. If an IRB or ethics committee reviewed your study, you will also be required to upload documentation from the IRB or ethics committee indicating that your study was approved or determined to be exempt.

The submitting author is responsible for including all co-author COI and disclosure information. Are you unsure about potential conflicts of interest among your co-authors? You can send an email to your co-authors requesting this information directly from the article submission process.

Conflicts of interest may involve:

- 3rd party payment or service for any aspect of the submitted work
- Relevant financial activities outside the submitted work
- Patents that could be considered broadly applicable to the research
- Any relationships not covered previously

Based on the information and disclosures provided in the submission, Cureus will automatically generate an [Ethics Statement and Conflict of Interest Disclosures](#) to be included alongside the published article. Please see the [Publication Ethics](#) and [Conflicts of Interest](#) sections of the [Author Guide](#) to view a detailed breakdown of required statements and disclosures.

### **Article**

Enter the main article content here. Article sections will vary depending on the article type selected earlier in the submission process. Do not compose your article directly in the text field. Instead, first write your article in the word processor of your choice and then copy and paste your article text into the appropriate section. Please do not include section names (e.g. Introduction, Materials C Methods, Results, etc.) as these are added automatically.

### **Previously Presented as Abstract or Poster**

If you previously presented your article as an abstract or poster, this must be mentioned in the introduction section of your Cureus submission. Please include the meeting or conference title and date. For example, "This article was previously presented as a meeting abstract at the 2020 AANS Annual Scientific Meeting on April 27, 2020."

### **Previously Posted to Preprint Server**

If you previously posted your article to a preprint server, this must be mentioned in the body of the article. For example, "This article was previously posted to the medRxiv preprint server on April 27, 2020." Medical research article submissions currently available on a preprint server will be accepted if they are not pending full publication elsewhere.

### **Text Formatting**

All medical research articles must adhere to **Cureus formatting styles and submission guidelines:**

- **No paragraph indentations or bulleted lists**
- **Only one line return after each paragraph**
- **Only one space between sentences**
- **Please remove any text styling before copying and pasting your text into the appropriate field**

### **Scientific Nomenclature**

Please adhere to [CDC guidelines for writing scientific nomenclature](#) when referring to topics like bacteria and genes. (Italics cannot be used in article titles.)

### **Conclusions**

The conclusions should be concise and exclude any data or other information that requires citations.

### **1-2**

### **paragraphs**

**Articles with 1-2 sentence conclusions will not be accepted.**

### **Numbers**

Numbers 1-9 should be spelled out in your Cureus submission, except for measurements (e.g. 7 mm). Numbers higher than nine should be entered numerically (10, 100, 463, 1,932, etc.).

### **Citations**

References should be cited using square brackets. Square brackets should not be used anywhere in your article except for the in-text citations. Reference citations may be placed mid-sentence or at the end of a sentence (but before the period).

If multiple references are cited in one place, please list them as follows: [1-4], [1,3], [5,9-12], etc. Footnotes are not permitted. Citations are not allowed in figures, tables, videos, or 3D model titles. They should instead be included in the media legend or table cells.

### Media

To add media to your article submission, place your cursor in the desired location in the text field and click one of the 'Insert Figure, Table, Video, or 3D model' buttons on the article section toolbar. You will then be prompted to upload the figure, paste or create the table, paste the video or 3D model URL, and add a title and optional legend.

25 media items per article limit

Our article submission guidelines prohibit media in the abstract, introduction, or conclusions sections, except for the introduction section in review articles.

Please visit our [Media Guide](#) for detailed instructions on adding each media type and examples of unacceptable media.

### Subheaders

In every submission, Cureus allows for three levels of subheaders:

**Major subheaders** should be formatted using the subheader style in the 'Styles' dropdown menu. Major subheaders should be in sentence case, i.e. the first word should be capitalized, and all other words should be in lowercase, except proper nouns and acronyms/initialisms (such as GBM, SRS, etc.).

**Minor subheaders** should be in title case and italicized. Both major and minor subheaders should be followed by a line return before the next paragraph begins.

If the medical research article you're submitting contains a **third level of subheader**, it should be in sentence case and lead off the paragraph, followed by a colon (e.g. Patient Zero: This patient exhibited signs of...).

### Formulas

Cureus supports LaTeX. During submission, you can build formulas using LaTeX. You can also copy/paste and convert your pre-prepared formulas. Please keep this in mind when preparing your manuscript.

### Appendices (Optional)

#### Miscellaneous

Please refer to [IBM Support](#) for information on how to cite IBM SPSS statistics or [Stata Support](#) for citing Stata software within the article body. (These do not require a corresponding reference entry.)

Any medical device or similar technology referenced in the text should be immediately followed by the manufacturer name and location in parentheses for the first instance in both the abstract and the body.

Brand name drugs should be treated as a proper noun, but generic brands should remain lowercase. All questionnaires that have been previously published must be properly cited in the article (mandatory). If the questionnaire is not Open Access, permission for its use must be obtained before submission. Questionnaires developed by the authors should be included within the article appendices.

### References

Creating references for article submission is simple with our automated converting tool. Please format all references in a text document according to the Cureus style guidelines before copying and pasting the list and selecting 'Convert references'.

Once all references have been converted, please preview (and edit as necessary) each reference to ensure it has been converted correctly. We'll do our best to detect each reference type based on its formatting, **but the conversion tool is not perfect and the results will require your review**.

When editing your converted references, please do not add punctuation at the end — punctuation will be added automatically. If you prefer, you can also enter your references one by one.

Please view the [References section](#) of the Cureus submission guide for more detailed instructions.

### Advisers

#### Adding Advisers

The submitting author must suggest at least five colleagues or mentors to act as potential advisers on the manuscript draft. Advisers provide valuable feedback and suggestions that can strengthen your work, but are not considered formal peer reviewers. Our editors will not consider adviser feedback when evaluating your manuscript for publication approval. Advisers are intended to serve

as a resource for authors and you may decide whether to incorporate their feedback into your manuscript.

#### **What about peer review?**

Six peer reviewers will be invited by the journal to review your manuscript with additional peer reviewers added as needed. The Cureus peer review panel consists of relevant specialists who have either volunteered for the panel or previously published as an author in Cureus. To prevent a potential conflict of interest, peer reviewers with the same listed affiliation as you or your co-authors will not be invited to review your manuscript. Submitted peer reviews lacking in constructive feedback will be rejected by Cureus editors.

#### **How many reviews do I need?**

Two completed peer reviews are required. You'll receive an email when the second review is submitted, at which point you can proceed with revisions and request publication, or wait for more peer reviews to be submitted. Adviser feedback is not required, and incorporating it into your article is optional.

#### **Summary**

The summary contains a section-by-section outline of your article. You can review each aspect of your article and jump directly to a specific section of the submission process if you'd like to make changes.

If any issues with the reference citations are detected, you will receive a notification and list of the citation or reference-related issues (e.g. missing citations, missing references, incorrectly formatted citations).

It's your responsibility to identify and address all listed issues to proceed to the next step and submit your article.

#### **Submit**

Please preview your article draft one last time to ensure everything is in order. You cannot submit your draft without first previewing your work. When you're sure the draft complies with our article submission guidelines, click the 'Submit my article' button.

Peer review invitation emails will be sent out, and the peer review process will begin when your article is approved during our preliminary editorial review.

Please refer to The [Cureus Publishing Process](#) section for a detailed description of what happens next in the [Cureus medical](#) research article submission process.

#### **Purchasing Preferred Editing Service or Uploading Third Party Editing Service Receipt**

If, after submission, you receive an email from Cureus stating that our Preferred Editing service is required, you will be prompted to enter your payment information and resubmit the article. Your article cannot be edited while deferred for Preferred Editing.

If, after submission, you receive an email from the Cureus journal stating that professional third-party language editing is required, you will be prompted to enter the name of the service and upload an invoice or receipt when resubmitting the revised article.