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Short Title: **DUSG for Verification of Renal Ischemia During Partial Nephrectomy**

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ABSTRACT

Introduction: Doppler ultrasonography (DUSG) enables intraoperative assessment of renal perfusion during partial nephrectomy. This study evaluated the feasibility of DUSG and compared its outcomes with indocyanine green (ICG) fluorescence imaging and a control group (CG) without intraoperative perfusion imaging.

Methods: We retrospectively analyzed 426 patients undergoing minimally invasive partial nephrectomy between 2018 and July 2025. Ischemia verification was performed using DUSG in 174 patients (41%) and ICG in 29 patients (7%). The control group included 223 patients (52%). Selection of imaging modality depended on surgeon preference and intraoperative findings. Perioperative, oncological, and functional outcomes were analyzed using one-way ANOVA and chi-square tests.

Results: No significant differences were observed in tumor size, BMI, warm ischemia time, blood loss, RENAL score, or complication severity assessed by the Clavien–Dindo classification. Selective clamping and clamp adjustment were significantly more frequent in the DUSG and ICG groups compared with controls (both $p < 0.001$). Positive surgical margin rates were low and comparable between groups.

Conclusion: Both DUSG and ICG represent safe and effective methods for ischemia verification; however, DUSG offers the advantages of lower cost, wider availability, and no risk of contrast-related adverse reactions, making it a practical option for routine clinical use.

Key words: partial nephrectomy, arterial occlusion, Doppler ultrasonography, Indocyanine green, fluorescence imaging, selective clamping, renal cell carcinoma

INTRODUCTION

Renal cell carcinoma (RCC) is the 14th most common cancer worldwide [1], with the Czech Republic consistently ranking among the countries with the highest incidence. According to the Czech National Cancer Registry, 3033 new cases were diagnosed in 2021. The rising incidence with stable mortality in developed countries is likely attributable to the widespread use of imaging modalities, enabling detection of early-stage tumors, particularly stage I [2].

The gold standard for the treatment of localized RCC is surgical treatment, either radical nephrectomy (RN) or partial nephrectomy (PN) [3]. Advances in surgical techniques, together with increasing surgeon expertise, have led to the development of minimally invasive approaches, primarily laparoscopic and robot-assisted procedures. Meta-analyses confirm the advantages of robot-assisted PN over the laparoscopy, particularly shorter warm ischemia time (WIT) and lower conversion rates, even in technically demanding and anatomically complex tumors [4–6].

PN is the preferred treatment for localized T1 renal tumors when technically feasible, with the aim of maximizing renal function preservation and minimizing the risk of chronic kidney disease [7,8]. The procedure is usually performed with temporary clamping of the main renal artery, however, alternatives include resection without clamping (the off-clamp technique) or selective clamping of segmental branches supplying the tumor [9,10]. According to the European Association of Urology (EAU), these alternatives are recommended only in selected cases, such as in patients with chronic kidney disease, a solitary kidney, or multifocal tumors [11].

In cases with complex vascular anatomy, challenging hilar dissection, or selective clamping, intraoperative imaging techniques can help to verify ischemia in the tumor area. This study evaluates our center's experience with Doppler ultrasonography (DUSG) and indocyanine green (ICG) fluorescence imaging for intraoperative ischemia assessment and compares outcomes with a control group (CG) without imaging.

While ICG fluorescence imaging is increasingly used in robot-assisted surgery, data regarding the use of DUSG for intraoperative perfusion assessment remain limited. Therefore, the primary aim of our study was to evaluate whether DUSG represents a safe and reliable method for ischemia verification during minimally invasive partial nephrectomy. These findings may be particularly relevant for centers with limited technical resources or without routine access to advanced fluorescence imaging systems.

METHODOLOGY

We retrospectively analyzed patients who underwent minimally invasive PN for tumors at the Urology Clinic of the University Hospital in Pilsen between 2018 and July 2025.

Patients who required conversion to open surgery or radical nephrectomy were excluded, as were those undergoing resection without renal hilum clamping.

A total of 426 patients were included. Intraoperative ischemia verification was performed using DUSG (n = 174; 41%) or fluorescence imaging with ICG Verdye® (1.25–2.5 mg; ICG; n = 29; 7%). The control group (CG) consisted of patients who underwent surgery without intraoperative imaging (n = 223; 52%).

Laparoscopic resection was performed in 149 patients (35%), while following introduction of the da Vinci Xi robotic system in June 2020, the majority of procedures were robot-assisted (n = 277; 65%). Seven patients (2%) underwent resection on a solitary kidney, and a retroperitoneoscopic approach was used in 9 cases (2%).

In our cohort, intraoperative perfusion assessment was used selectively, mainly in cases with complex vascular anatomy, challenging hilar dissection, selective clamping, or when ischemia was not clearly identifiable on macroscopic inspection. The choice of imaging modality (DUSG vs. ICG) primarily depended on the operating surgeon's preference and experience. At our institution, ICG fluorescence imaging was used by a limited number of surgeons, whereas DUSG represented the preferred modality for routine intraoperative ischemia verification. Tumor complexity was evaluated using the RENAL nephrometry score and postoperative renal function was assessed using estimated glomerular filtration rate (eGFR).

Selective clamping was defined as clamping of segmental branches supplying the tumor. Clamp adjustment was defined as any intraoperative modification of vascular control, including repositioning of the clamp, addition of a clamp, or conversion from selective to global ischemia.

During the study period, a robotic surgical system (da Vinci Xi) was gradually introduced at our institution. To account for potential confounding related to this transition and the associated learning curve, subgroup analyses were performed separately for laparoscopic and robot-assisted procedures.

For statistical evaluation, continuous variables were compared across the three groups using one-way analysis of variance (ANOVA) with Tukey post-hoc analysis. Categorical variables were analyzed using the chi-square test. A p-value < 0.05 was considered statistically significant.

RESULTS

An overview of the definitive histological results is provided in Table 1.

No statistically significant differences were observed between the study groups regarding BMI, tumor size, warm ischemia time, blood loss, RENAL nephrometry score, or overall complication severity assessed by the Clavien–Dindo classification in the overall cohort (Tables 2–4).

In contrast, significant differences were identified in patient age, operative time, and postoperative renal function assessed by eGFR. Patients in the ICG group were significantly younger than those in the DUSG and control group ($p < 0.001$). Operative time also differed significantly between groups ($p = 0.002$), with the shortest procedures observed in the ICG cohort. Post-hoc analysis demonstrated significant differences between the ICG and DUSG groups, whereas the control group did not differ significantly from either imaging modality. A statistically significant difference in postoperative eGFR was observed between groups ($p = 0.046$), with higher postoperative values in the ICG cohort.

Selective clamping was performed significantly more frequently in patients undergoing intraoperative perfusion assessment than in the control group, particularly in the ICG cohort ($p < 0.001$). Similarly, the need for intraoperative clamp adjustment was significantly higher in the DUSG and ICG groups compared with controls ($p < 0.001$).

The rate of positive surgical margins (pR1) was low and did not differ significantly between groups, supporting comparable oncological safety across all approaches.

During the study period, robot-assisted surgery was introduced at our institution, and therefore subgroup analyses were perfomed separately for laparoscopic and robot-assisted procedures. In the laparoscopic subgroup, perioperative outcomes were generally comparable between groups, with the exception of a significantly higher Clavien–Dindo score in the DUSG group ($p = 0.007$). However, this difference was not observed in the overall cohort or in the robot-assisted subgroup. In the robot-assisted subgroup, patients in the ICG cohort remained significantly younger than those in the DUSG and control groups, while no significant differences were identified in tumor complexity, operative time, warm ischemia time, renal function, or complication rates. Importantly, the significantly higher rates of selective clamping and reclamping in the DUSG and ICG groups persisted in both subgroup analyses.

In one patient, both DUSG and ICG fluorescence imaging were used simultaneously. The patient presented with two renal arteries, and residual perfusion was detected by DUSG following sequential clamping of each artery. Subsequent administration of 2.5 mg Verdye® confirmed ischemia of the tumor-bearing lower renal pole during clamping of the lower pole artery. Histopathological examination revealed angiomyolipoma.

Detailed perioperative and subgroup analyses are summarized in Tables 2–4.

DISCUSSION

Minimally invasive PN has become the standard treatment modality for localized renal carcinoma, particularly for tumors up to 7 cm (stage T1) [12]. The introduction of robot-assisted surgery has significantly expanded the technical capabilities of surgeons, improving resection precision, the safety of vascular clamping, and intraoperative visualization.

Preoperative diagnosis and treatment planning

Safe performance of PN requires careful preoperative preparation, including evaluation of tumor size, location, its relationship to vascular structures, and anatomical conditions within the renal hilum.

The current gold standard for preoperative imaging remains contrast-enhanced spiral computed tomography (CT) with angiography. In anatomically complex cases with challenging vascular supply, three-dimensional (3D) reconstructions can provide further detail, supporting optimal surgical planning [13]. In patients with contraindications to CT or in cases where the presence of a tumor thrombus is suspected, magnetic resonance imaging (MRI) with contrast administration represents a suitable alternative [14,15].

Future advances in 3D modeling, augmented reality, and CT or MRI-based intraoperative navigation may further improve surgical techniques and allow greater individualization of vascular approaches [16,17].

Vascular clamping strategy

One of the key determinants of postoperative renal function is the duration and extent of warm ischemia. In selected patients, off-clamp or selective clamping techniques may reduce ischemic injury to the renal parenchyma [18–20]. Ideally, the duration of warm ischemia should not exceed 25 minutes in order to preserve postoperative kidney function as much as possible [21,22]. Nonetheless, some studies (e.g., Sharma et al.) have shown no significant differences in renal function outcomes between different clamping strategies [23]. In our cohort, selective clamping was performed significantly more frequently in patients undergoing intraoperative perfusion assessment using DUSG or ICG. Similarly, the need for intraoperative clamp adjustment was significantly higher in these groups, particularly in the ICG cohort. These findings suggest that intraoperative perfusion imaging may improve the identification of incomplete ischemia and facilitate immediate correction of vascular control during selective clamping. A statistically significant difference in postoperative eGFR was observed in the ICG group. Nevertheless, evaluation of renal functional outcomes was limited by the absence of consistently available

preoperative renal function data, which prevented assessment of postoperative renal function decline. Furthermore, the ICG cohort was relatively small and consisted of significantly younger patients, both of which may have influenced postoperative eGFR values.

Intraoperative imaging techniques

The refinement of minimally invasive surgical techniques is aimed at three key objectives: reducing the duration of warm ischemia, ensuring oncological radicality (negative surgical margins), and minimizing intraoperative complications [24]. To support these goals, intraoperative imaging modalities are increasingly employed. Commonly used methods include Doppler ultrasonography (DUSG), contrast-enhanced ultrasonography (CEUS), and indocyanine green (ICG) fluorescence technology [25–27]. In our cohort, intraoperative perfusion imaging was preferentially used in anatomically complex cases, which likely contributed to the higher frequency of clamp adjustments observed in both the DUSG and ICG groups.

Recent research has also explored other fluorescent agents, such as OTL38 (On Target Laboratories LLC., West Lafayette, IN, USA), which targets folate receptors and demonstrates distinct fluorescence patterns between tumor and normal tissue [28]. Additional experimental agents are being investigated to enhance intraoperative tumor detection and improve assessment of resection radicality, even in endophytic lesions [29,30]. In parallel, advanced technologies such as 3D modeling and augmented reality are under development, enabling CT-based spatial reconstructions of the kidney to be projected directly into the surgical field and thereby improving intraoperative navigation [16,17,31].

Selective clamping of the renal artery

One of the key determinants of postoperative renal function is the duration of warm ischemia (WIT). The strategy of selectively clamping segmental branches of the renal artery was developed specifically to minimize ischemic damage to the parenchyma. In such cases, intraoperative visualization of perfusion can be of substantial benefit. Doppler ultrasonography (DUSG) has long been used in partial nephrectomy. It enables more precise tumor localization, identification of vascular structures, and detection of accessory arteries not visualized during preoperative imaging (Fig. 1). Several studies have demonstrated that DUSG can shorten ischemia time and enhance procedural safety without increasing morbidity [32–35]. According to Hyams et al., Doppler mapping also facilitates faster hilar dissection and, in some cases, leads to intraoperative adjustment of vascular clamps during selective clamping [36].

The use of ICG is becoming increasingly widespread, particularly in robotic surgery, where it provides detailed real-time visualization of perfusion with high sensitivity and without requiring tissue contact (Fig. 2) [37]. Fluorescence imaging with ICG has been shown to reduce ischemia time and increase the accuracy of vascular clamping, as reported by Krane et al. and Yang et al. [38–40]. Similar findings were described by Wang et al., who demonstrated particular advantages of ICG in patients with higher RENAL scores [41].

Both DUSG and ICG represent effective methods for intraoperative perfusion monitoring, although each technique has specific advantages and limitations. DUSG is inexpensive, widely available, and does not require specialized equipment. Conversely, ICG fluorescence imaging offers highly sensitive visualization of tissue perfusion but requires dedicated near-infrared imaging systems and administration of a contrast agent. Although ICG is generally considered safe and severe adverse events are rare, allergic, anaphylactic, and cardiovascular reactions, including hypotension and tachycardia, have been described in the literature, particularly in patients with hypersensitivity to iodinated compounds or after higher cumulative doses [42–44]. Importantly, DUSG may represent a practical alternative for centers without access to fluorescence imaging technology.

Several limitations of this study should be acknowledged. First, this was a retrospective single-center analysis and therefore subject to selection bias. The choice of intraoperative imaging modality was left to the discretion of the operating surgeon. In addition, the ICG cohort was relatively small and markedly unbalanced compared with the DUSG and control groups, which limits the statistical power and robustness of comparisons involving ICG and may have influenced some observed differences. Second, robotic surgery was gradually introduced during the study period, representing a potential source of confounding and therefore prompting separate subgroup analyses for laparoscopic and robot-assisted procedures. Finally, the absence of complete preoperative renal function data prevented evaluation of postoperative renal function decline and limited interpretation of eGFR outcomes.

CONCLUSION

Our findings confirm that DUSG and fluorescence imaging with ICG are both reliable and safe techniques for intraoperative assessment of renal perfusion during PN. Both modalities allow for early detection of incomplete ischemia and timely correction of vascular clamping, without compromising the oncological radicality of the procedure.

Although ICG fluorescence imaging is increasingly integrated into robotic surgery platforms, DUSG remains a simple, widely available, and cost-effective technique that can be readily implemented in routine clinical practice, including centers without access to near-infrared fluorescence technology.
Despite the retrospective design and potential selection bias, our findings support DUSG as a valid alternative for intraoperative ischemia verification during partial nephrectomy.

STATEMENT OF ETHICS

This study was conducted in accordance with the Declaration of Helsinki and approved by Ethics Committee of The University Hospital and the Faculty of Medicine, Charles University in Pilsen - approval: 182/25.
The study was not registered as a clinical trial because it was a retrospective observational analysis. The requirement for informed consent was waived by the ethics committee due to the retrospective, non-interventional design of the study and the use of anonymized data.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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AUTHOR CONTRIBUTIONS

Adriena Bartoš Veselá contributed to study conceptualization, methodology, data analysis, and writing of the original draft.
Milan Hora contributed to study conceptualization, supervision of the project, and critical revision of the manuscript.
Hana Sedláčková contributed to manuscript revision and editing of early drafts.
Jiří Kolář, Tomáš Pitra, Petr Stránský Jr., Tomáš Ürge, and Ivan Trávníček contributed to patient care, data acquisition, and clinical support essential for this study.
Jiří Ferda and Kristýna Pivovarčíková contributed domain-specific expertise and provided access to data from collaborating specialties.
All authors reviewed and approved the final version of the manuscript.

DATA AVAILABILITY STATEMENT

The datasets generated and analyzed during the current study are not publicly available due to GDPR and patient privacy restrictions, but are available from the corresponding author on reasonable request.

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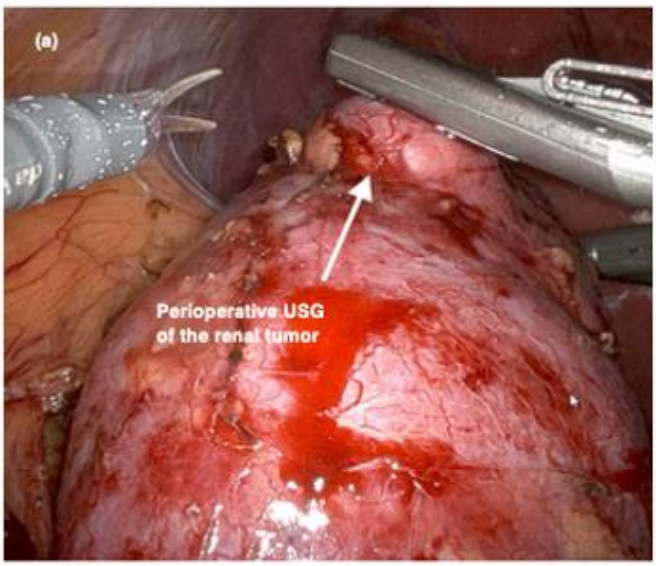
FIGURE LEGENDS

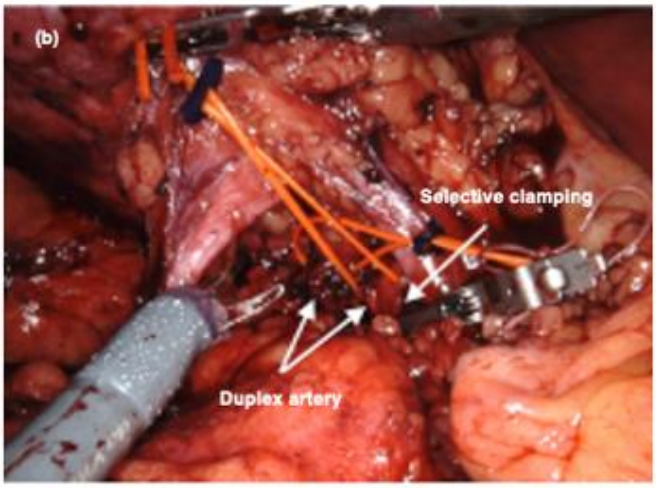
Fig. 1. Verification of renal perfusion using Doppler ultrasonography (DUSG).

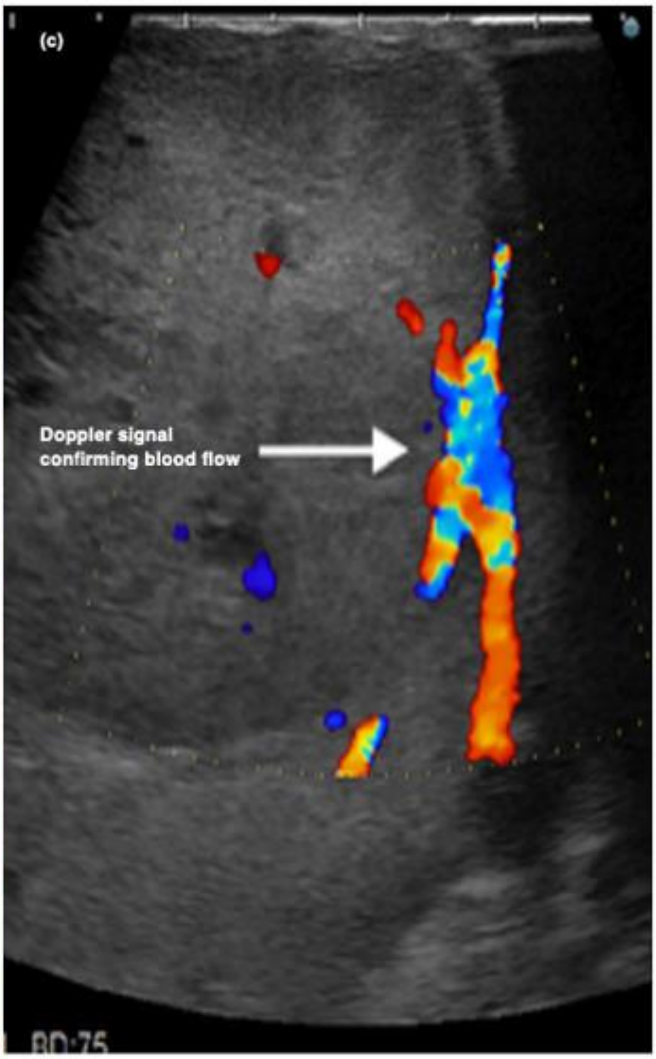
(a) Perioperative ultrasonography of the renal tumor.
(b) Duplex renal artery and selective clamping.
(c) Doppler signal confirming residual blood flow.

Fig. 2. Verification of renal perfusion using indocyanine green (ICG) fluorescence imaging.

(a) Renal tumor and duplex renal artery during hilar dissection.
(b) Perfusion boundary visualized using ICG fluorescence imaging.







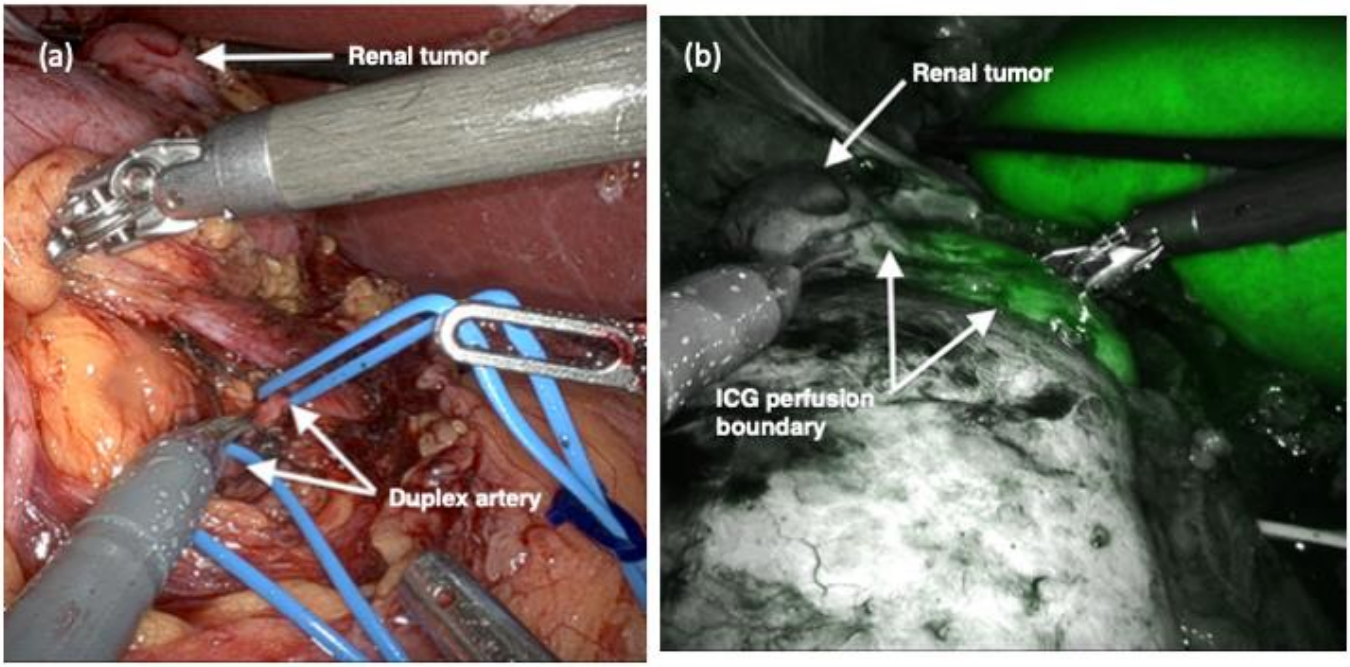


Table 1. Histological Subtypes of Operated Tumors

Histological subtype	n	%
Clear cell renal cell carcinoma	247	58%
Papillary renal cell carcinoma	69	16%
Renal oncocytoma	37	9%
Chromophobe renal cell carcinoma	17	4%
Angiomyolipoma	19	4%
Benign lesions	11	3%
Multilocular cystic renal neoplasm of low malignant potential	5	1%
Eosinophilic, solid and cystic renal cell carcinoma	5	1%
Low-grade Oncocytic Tumor	3	1%
ELOC-mutated renal cell carcinoma	1	0%
Others	12	3%

Table 2. Overall cohort characteristics
Values are presented as mean ± SD or n (%)

Parameter	DUSG (n=174)	ICG (n=29)	CG (n=223)	p-value
Age (years)	64.16 ± 10.59[a]	57.28 ± 12.50[b]	65.52 ± 10.29[a]	**<0.001**
BMI (kg/m²)	30.27 ± 5.41	28.84 ± 3.91	29.87 ± 4.99	0.352
Tumor size (mm)	30.25 ± 11.88	29.86 ± 10.96	30.46 ± 11.58	0.960
Time of surgery (min)	118.39 ± 27.60[a]	99.76 ± 25.63[b]	112.33 ± 28.01[a]	**0.002**
Warm ischemia time (min)	15.39 ± 5.39	15.21 ± 4.85	15.34 ± 5.50	0.985
Blood loss (ml)	136.58 ± 165.09	152.07 ± 197.31	141.61 ± 194.23	0.903
eGFR (ml/min/1.73 m²)	67.26 ± 22.26[a]	77.62 ± 23.52[b]	67.15 ± 17.99[a]	**0.046**
Clavien–Dindo	1.40 ± 0.72	1.34 ± 0.67	1.30 ± 0.58	0.376
RENAL score	6.59 ± 1.92	6.83 ± 1.79	6.61 ± 1.93	0.832
Selective clamping	47 (27.0%)	14 (48.3%)	23 (10.3%)	**<0.001**
Reclamping	41 (23.6%)	18 (62.1%)	6 (2.7%)	**<0.001**
pR1	12 (6.9%)	3 (10.3%)	28 (12.6%)	0.178

Continuous variables were analyzed using one-way ANOVA with Tukey post-hoc analysis. Categorical variables were comp
using the chi-square test. Different superscripts (a,b) indicate statistically significant differences between groups in post-hoc a

Table 3. Laparoscopic subgroup
Values are presented as mean ± SD or n (%)

Parameter	DUSG (n=22)	ICG (n=20)	CG (n=107)	p-value
Age (years)	64.84 ± 11.82	59.39 ± 12.97	66.14 ± 9.42	**0.029**
BMI (kg/m²)	30.05 ± 5.46	29.18 ± 3.66	30.25 ± 4.89	0.663
Tumor size (mm)	31.59 ± 9.96	31.10 ± 11.51	28.52 ± 10.14	0.319
Time of surgery (min)	93.45 ± 18.82	93.25 ± 23.39	103.40 ± 28.70	0.123
Warm ischemia time (min)	14.91 ± 4.30	14.20 ± 4.26	15.23 ± 5.77	0.729
Blood loss (ml)	151.6 ± 159.4	140.0 ± 185.6	121.3 ± 177.1	0.725
eGFR (ml/min/1.73 m²)	70.17 ± 26.10	78.85 ± 22.60	67.98 ± 17.80	0.118
Clavien–Dindo	1.77 ± 1.10[a]	1.30 ± 0.47[b]	1.29 ± 0.55[b]	**0.007**
RENAL score	6.50 ± 1.74	6.95 ± 1.64	6.68 ± 1.86	0.720
Selective clamping	5 (22.7%)	9 (45.0%)	11 (10.3%)	**<0.001**
Reclamping	6 (27.3%)	13 (65.0%)	3 (2.8%)	**<0.001**
pR1	0 (0%)	2 (10.0%)	12 (11.2%)	0.258

Continuous variables were analyzed using one-way ANOVA with Tukey post-hoc analysis. Categorical variables were comp
using the chi-square test. Different superscripts (a,b) indicate statistically significant differences between groups in post-hoc a

Table 4. Robot-assisted subgroup
Values are presented as mean ± SD or n (%)

Parameter	DUSG (n=152)	ICG (n=9)	CG (n=116)	p-value
Age (years)	64.06 ± 10.44[a]	52.60 ± 10.58[b]	64.95 ± 11.04[a]	**0.004**
BMI (kg/m²)	30.30 ± 5.42	28.10 ± 4.55	29.53 ± 5.06	0.282
Tumor size (mm)	30.06 ± 12.15	27.11 ± 9.68	32.25 ± 12.54	0.228
Time of surgery (min)	121.99 ± 26.83	114.22 ± 25.68	120.54 ± 24.76	0.649
Warm ischemia time (min)	15.46 ± 5.54	17.44 ± 5.57	15.44 ± 5.26	0.556
Blood loss (ml)	134.4 ± 166.3	178.9 ± 230.7	160.3 ± 207.8	0.463
eGFR (ml/min/1.73 m²)	66.90 ± 21.81	75.00 ± 26.79	66.43 ± 18.20	0.524
Clavien–Dindo	1.34 ± 0.63	1.44 ± 1.01	1.32 ± 0.61	0.837
RENAL score	6.61 ± 1.95	6.56 ± 2.19	6.56 ± 2.00	0.981
Selective clamping	42 (27.6%)	5 (55.6%)	12 (10.3%)	**<0.001**
Reclamping	35 (23.0%)	5 (55.6%)	3 (2.6%)	**<0.001**
pR1	12 (7.9%)	1 (11.1%)	16 (13.8%)	0.294

Continuous variables were analyzed using one-way ANOVA with Tukey post-hoc analysis. Categorical variables were comp
using the chi-square test. Different superscripts (a,b) indicate statistically significant differences between groups in post-hoc a