



Oncological outcome audit of multivisceral resections for primary colorectal cancer: a single centre experience

Pregled onkoloških rezultata multivisceralnih resekcija kod primarnog kolorektalnog karcinoma: iskustvo jednog centra

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Abstract

Background/Aim. Colorectal cancer still presents a major health problem, with around 10% of patients in whom the tumor invades surrounding structures or organs. These patients are usually challenging even for an experienced colorectal surgical team. The decision for performing multivisceral resection (MVR) is often made intraoperatively, with no sufficient data on the tumor and patient condition. The percentage of perioperative morbidity and mortality is high and oncological outcome is often unfavorable. The aim of this study was to investigate the poor oncological outcome risk factors after MVR in the patients with colorectal carcinoma. **Methods.** This was a retrospective analysis of patients operated at the Department for Colorectal Surgery of the First Surgical Clinic, Clinical Centre of Serbia, Belgrade. The *en bloc* multivisceral resection for the primary adenocarcinoma of the colon and rectum was uniformly performed. Data were collected in prospectively designed database. Follow-up period was minimum 2 years. The patients were analyzed in terms of histopathological, demographical and follow-up data. Survival and time to recurrence were evaluated using the Kaplan–Meier method and the log-rank test. **Results.** Two hundred and thirteen patients were included in the study. Their mean age was 59.9 ± 12.0 years. The follow-

up period was 33.8 ± 29 months. Histopathology confirmed the true tumor infiltration of surrounding organ/structure in 126 (59.2%) patients. The R0 resection was confirmed in 173 (81.2%) patients. Five-year overall survival was 43.4%. Five-year survival for colon patients was 45.9% and in the rectal cancer group 40.9%. In the N0 group of patients, the overall survival in 5-year period was 66.7%. The N1 and N2 status proved the adverse effect on survival (overall 5-year survival 31.3% and 15.9%, respectively). The five-year local recurrence rate in the R0 group of patients was 17.7% and the percentage of distant metastases was 66.3%. **Conclusion.** The multivisceral resections are demanding procedures requiring a highly specialized surgical team and a high volume hospital. The oncological outcome of these procedures is still unfavorable. In the cases with the node positive disease, or the R1 resection, the perspective is poor. On the other hand, in the absence of these unfavorable factors, we can expect a good oncological outcome. More meticulous preoperative staging and aggressive preoperative treatment can further improve the results.

Key words: colorectal neoplasms; neoplasm invasiveness; neoplasm staging; surgical procedures, operative; prognosis.

Apstrakt

Uvod/Cilj. Kolorektalni karcinom još uvek predstavlja veliki zdravstveni problem sa oko 10% slučajeva kod kojih je tumor zahvatio okolne strukture/organe. Kompleksno lečenje ovih bolesnika je izazov, čak i u specijalizovanim centrima. Odluka o izvođenju multivisceralne resekcije (MVR) se često donosi intraoperativno, bez dovoljno informacija o tumorskom statusu ili samom bolesniku. Perio-

perativni morbiditet i mortalitet je visok, a onkološki ishod lečenja je često nepovoljan. Cilj rada je bio da se izlože faktori rizika lošeg ishoda nakon MVR kod bolesnika sa kolorektalnim karcinomom. **Metode.** Sprovedena je retrospektivna studija bolesnika operisanih na III Odeljenju, Prve hirurške klinike Kliničkog centra Srbije. *En bloc* MVR zbog primarnog adenokarcinoma kolona i rektuma je bila učinjena kod svih bolesnika. Podaci su bili prikupljeni u prospektivno dizajniranoj bazi podataka. Postoperativno

praćenje je iznosilo minimum dve godine. Analiza je obuhvatala patohistološke, demografske i podatke postoperativnog praćenja. Preživljavanje i vreme do recidiva bolesti je procenjavano na osnovu Kaplan-Meier i long-rank testa. **Rezultati.** Dvesta trinaest bolesnika je bilo uključeno u studiju. Prosek godina iznosio je $59,9 \pm 12,0$, a praćeni su prosečno $33,8 \pm 29$ meseci. Patohistološki, tumorska infiltracija okolnih organa/struktura dokazana je kod 126 (59,2%) bolesnika. R0 resekcija je potvrđena kod 173 (82,1%) bolesnika. Ukupno petogodišnje preživljavanje je iznosilo 43,4%. Kod bolesnika sa karcinomom kolona preživljavanje je iznosilo 45,9%, a kod onih sa karcinomom rektuma 40,9%. Ukupno petogodišnje preživljavanje u N0 grupi bilo je 66,7%. N1 i N2 kategorije su imale loš uticaj na petogodišnje preživljavanje (ukupno preživljavanje 31,3% i 15,9%, respektivno). Petogodišnji lokalni recidiv u R0 grupi iznosio je 17,7%, a procenat udaljenih metastaza je bio

66,3%. **Zaključak.** Multivisceralne resekcije su zahtevne procedure, zahtevaju visoko specijalizovan hirurški tim u ustanovi sa velikim brojem takvih slučajeva. Onkološki rezultat ovih operacija je još uvek nezadovoljavajući, bez velikih varijacija u odnosu na lokalizaciju bolesti (kolon/rektum). Kod slučajeva sa pristunim nodalnim metastazama, ili kod onih sa R1 resekcijom, perspektiva je veoma loša. Sa druge strane, kod onih gde ne postoje navedeni faktori rizika, možemo da očekujemo razumno dobar rezultat lečenja. Rezultate je moguće unaprediti sprovođenjem detaljnog preoperativnog određivanja stadijuma bolesti i primenom agresivne neoadjuvantne terapije.

Ključne reči:

kolorektalne neoplazme; neoplazme, invazivnost; neoplazme, određivanje stadijuma; hirurgija, operative procedure; prognoza.

Introduction

Colorectal cancer, despite all efforts made in the early discovery, preoperative therapy, surgery and adjuvant treatment, still presents the major health problem^{1,2}. In countries with developed screening programs, early colorectal cancer becomes an important issue with almost 20% –25% of all treated patients. On the other side, surgeons still have at hands a considerable number of patients with advanced disease³. Among these, the patients with locally advanced tumors are of special interest to us. By using the good pre-treatment staging, neo and adjuvant treatment, and most importantly, the high quality surgery, the cure of the disease is still achievable. We have around 10% of patients with tumor invading the surrounding structures or organs, i.e., T4b adenocarcinomas³. These patients are usually challenging to treat even for an experienced colorectal surgical unit^{2,4-7,9}. The reasons for this are numerous: the decision for performing multivisceral resection (MVR) is made intraoperatively with no sufficient data on the tumor and patient condition, the percentage of perioperative morbidity and mortality is high and finally, the oncological outcome is often unfavourable. Many explanations are offered, but it still remains a matter of debate among experts. The *en bloc* resection is a well-established method of choice. Any fragmentation of partial resection is followed by a poor oncological outcome with unacceptable morbidity and mortality, thus, we have to avoid the emergency of unplanned MVR in order to achieve the good treatment result. Meticulous preoperative staging is of paramount importance. In addition, we have to be aware of unfavourable prognostic factors that would prevent us of performing, or lead us to employ the neoadjuvant approach prior to the MVR. Postoperatively, the group of high-risk patients is the candidate for the intensive adjuvant treatment and more aggressive follow-up regimen. Among mentioned above, the impact of lymph node metastases on the treatment outcome⁶⁻⁸ was discussed controversially in a number of papers and was described to be associated with an adverse outcome.

Having at hand relatively large population of patients with locally advanced colon and rectal carcinomas in our unit where the MVR was performed, we performed a retrospective analysis of all patients operated between 1995 and 2011.

The type of operation and details of pathological report were analysed in order to establish the risk factors for a poor oncological outcome after the MVR.

Methods

The study was a retrospective analysis of prospectively collected data of consecutive cohort of patients in the period between September 1995 and December 2011. All patients were operated at the Department for Colorectal Surgery of the First Surgical Clinic, Clinical Centre of Serbia, Belgrade. The procedures were performed by the same surgical team and included the *en bloc* MVR for the primary adenocarcinoma of colon and rectum. The patients with distant metastases and those with the intraoperative tumor fragmentation were excluded. The study was approved by the Ethics Committee of the Faculty of Medicine in Belgrade. The preoperative workup included: endoscopy with biopsy, cystoscopy, ultrasound, pelvic/abdominal computed tomography/magnetic resonance imaging (CT/MRI).

The patients were operated following a standardized open approach with high ligation of the corresponding lymphovascular bundle. Additionally, if the infiltration of adjacent organs was suspected, or the mobilization, or the sharp dissection was not feasible, a primary MVR was performed. The procedures were classified according to the primary colorectal operation regardless of the extent of additional resection. The sixth edition of the Union for International Cancer Control (UICC) classification from 2002 was used to categorize colorectal adenocarcinomas. Rectal cancer was diagnosed according to the distance, measured by a rigid proctoscope (first 15 cm). In the patients with rectal cancer, a neoadjuvant treatment was not standardized according to the modern guidelines. Only the most advanced cases fit for this mode of treatment, selectively received neoadjuvant chemoradiotherapy. The majority

of patients in the neoadjuvant treatment group were planned for abdominoperineal amputation.

Patients' histopathology and operation data were collected in prospectively designed database. The follow-up period was minimum 2 years according to the standardized protocol.

The data was evaluated by using the descriptive statistical methods. The patients with the MVR were analysed in terms of the histopathological, demographical and follow-up data. The survival and time to recurrence were evaluated by using the Kaplan–Meier method and the log-rank test. The *p* value < 0.05 was considered significant.

Results

Initially, 213 patients were included in the study. Their basic characteristics are shown in Table 1.

Table 1
Clinical and histopathological features of patients with multivisceral resections for primary colorectal carcinoma

Characteristics of patients	Multivisceral reactions n (%)
Sex	
female	94 (44.1)
male	119 (55.9)
Tumor localization	
colon	107 (50.2)
rectum	106 (49.8)
TNM status	
T3	87 (40.8)
T4	126 (59.2)
N0	95 (44.6)
N1	50 (23.5)
N2	68 (31.9)
N1 + N2	118 (55.4)
R status	
R0	173 (81.2)
R1	40 (18.8)

TNM staging system of malignant neoplasms – tumor-lymph node-metastasis.

The mean age was 59.9 ± 12.0 years. The average follow-up period was 33.8 ± 29 months. A total of only 22 (20.75%) patients received the neoadjuvant treatment (the

rectal cancer patients). The number of colon and rectum cancer patients was comparable, almost equal (107 vs. 106, respectively). The most frequently, MVR was performed in the patients with sigmoid cancer. MVR involved the partial, or complete removal of single additional organ in 129 (60.6%) patients. The most commonly affected organ was the urinary bladder in 47 (22.1%) patients. The partial resection of the small intestine was necessary in 44 (20.7%) patients, and the abdominal wall was resected in 62 (29.1%) patients. The data are shown in Table 2. The infiltration of removed organs/structures was comparable to the overall infiltration rate of around 59%. This percentage was roughly present when analysing percentage of resected/infiltrated organs (Table 2).

Table 2
List and number of the resected and infiltrated organs

Organs	Resected organs n (%)	Tumor infiltration present n (%)
Pelvic wall	10 (4.69)	4 (1.88)
Abdominal wall	62 (29.11)	42 (19.72)
Diaphragm	3 (1.41)	1 (0.47)
Liver	8 (3.76)	6 (2.82)
Gallbladder	5 (2.35)	2 (0.94)
Duodenum	4 (1.88)	2 (0.94)
Pancreas	8 (3.76)	6 (2.82)
Stomach	3 (1.41)	2 (0.94)
Spleen	9 (4.23)	3 (1.41)
Kidney	3 (1.41)	2 (0.94)
Appendix	15 (7.04)	8 (3.76)
Other parts of colon	1 (0.47)	1 (0.47)
Small intestine	44 (20.66)	31 (14.55)
Urinary bladder	47 (22.07)	32 (15.02)
Uterus	17 (7.98)	10 (4.69)
Adnexa	30 (14.08)	13 (6.10)
Ureter	5 (2.35)	2 (0.94)
Vagina	30 (14.08)	17 (7.98)
Prostate	18 (8.45)	10 (4.69)
Sem. vesicles	23 (10.80)	9 (4.23)
Sacrum	9 (4.23)	2 (0.94)
Other	5 (2.35)	1 (0.47)

Sixteen (7.5%) patients died in the first month after the operation. The procedures and average number of lymph nodes harvested are presented in Table 3.

Table 3
List of performed procedures and the average number of lymph nodes harvested

Type of surgical procedure	Surgical procedure n (%)	Average number (n) of lymph nodes harvested
Low anterior resection of the rectum	49 (23.01)	28.94
Resection of the rectum with partial mesorectal excision	39 (18.31)	28.44
Abdominoperineal resection of the rectum	35 (16.43)	20.34
Hartmann's procedure	27 (12.68)	26.63
Right hemicolectomy	28 (13.15)	28.64
Left hemicolectomy	11 (5.16)	30.09
Subtotal colectomy	7 (3.29)	47.00
Total pelvic exenteresis	5 (2.35)	25.40
Partial resection of the colon	5 (2.347)	17.60
Total colectomy	4 (1.88)	59.71

Table 4

Oncological outcomes, overall, according to localization (colon/rectum) and two favorable categories T3N0R0

Neoplasm	5-year OS (%)	5-year DFS(%)	5-year LR(%)	5-year DM(%)
Overall	43.40	31.01	26.75	65.29
Colon	45.97	34.40	25.90	62.67
Rectum	40.99	27.63	27.83	67.85
Colon T3N0R0	82.63	49.62	17.93	20.18
Rectum T3N0R0	87.50	71.09	6.20	22.22

OS – overall survival; DFS – disease free survival; LR – local recurrence; DM – distant metastases.

The histopathology exam confirmed the true tumor infiltration of the surrounding organ /structure in 126 (59.2%) patients. We were not able to confirm the true tumor infiltration in 87 (40.8%) cases – the R0 resection was confirmed in 173 (81.2%) patients (Table 1).

We analysed the prognostic factors overall and cancer-specific survival, time to local/distant recurrence.

Of interest to us, in terms of oncological outcome, was the group of patients with the favourable prognostic factors, i.e., with no nodal deposits and R0 resection. The results in the favourable categories, for colon and rectum carcinomas, are presented in Table 4.

The five-year overall survival was 43.4% (Figure 1), 45.9% for the colon patients and 40.9% for the patients from the rectal cancer group. The T stage proved to influence the oncological outcome of MVR and a significant difference was noted between the T3 and T4 tumors in terms of overall survival (OS) (60.03% and 32.97% at 5 years, respectively) (Figure 2). In the N0 group of patients, the situation was significantly better since OS in the five-year period was 66.7%. The N1 and N2 status proved the adverse effect on survival (overall survival 31.3% and 15.9% respectively) and no patients in this stage lived for 5 years. These results include both the R0 and R1 patients (Figure 3). The local recurrence rate in the R0 group of patients was 17.7% (Figure 4), and the percentage of distant metastases in the five-year period was 66.3% (Figure 5).

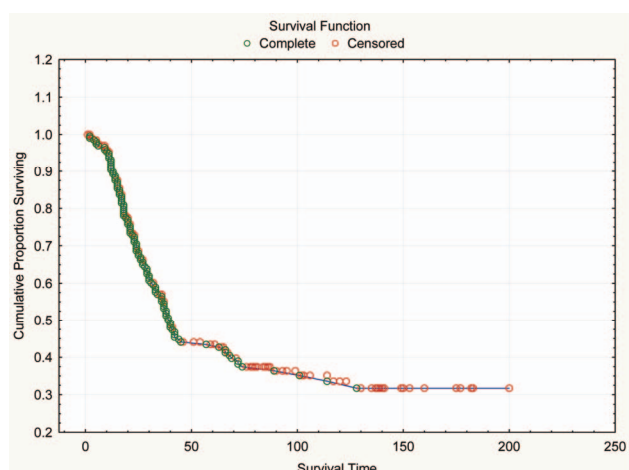


Fig. 1 – Kaplan-Meier curve – overall survival (43.4%) at 60 months.

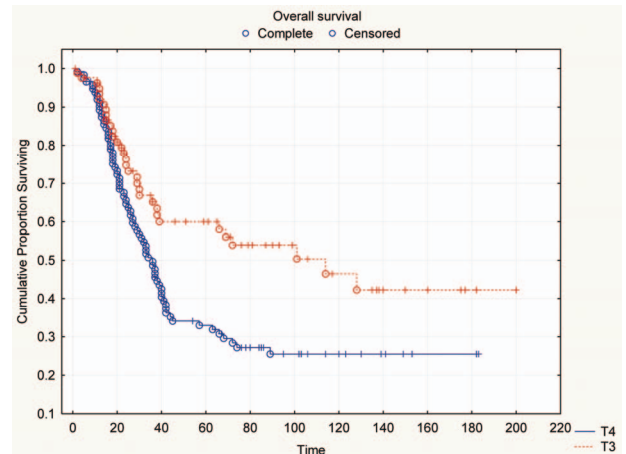


Fig. 2 – Kaplan-Meier curve – Overall survival according to the T stage.

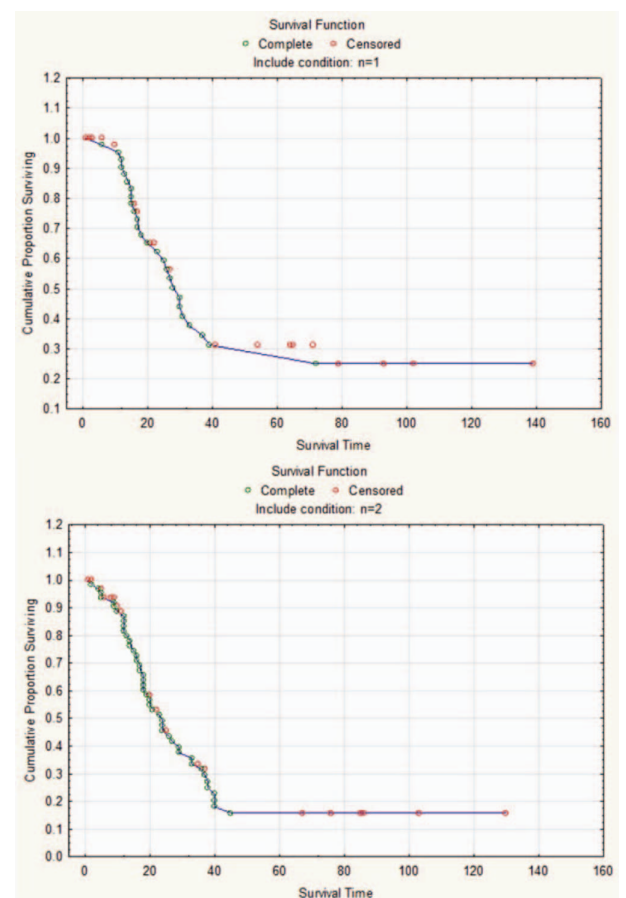


Fig. 3 – Kaplan-Meier curve – overall five-year survival in patients with the N1 and N2 status (31.3% and 15.9%, respectively).

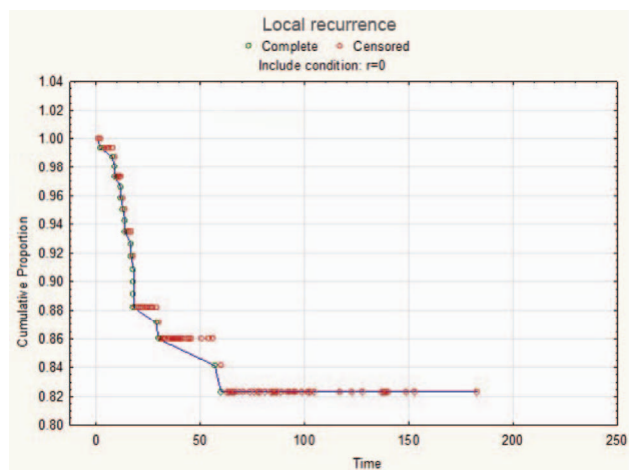


Fig. 4 – Kaplan-Meier curve – the local recurrence for the R0 resections trend. The local recurrence at 5 years – 17.7%.

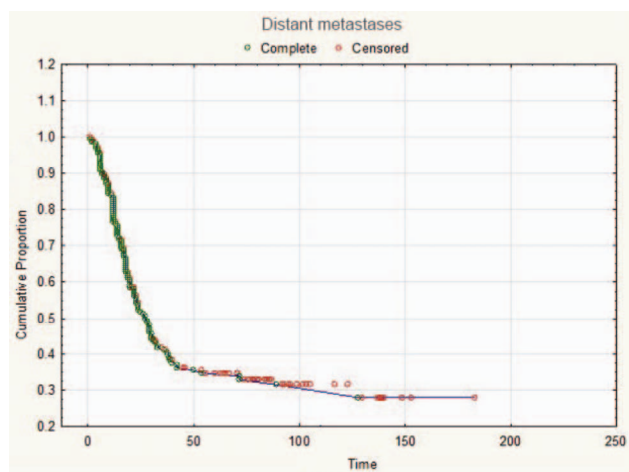


Fig. 5 – Kaplan-Meier curve – the distant metastasis trend. Distant metastases at 5 years – 66.3%.

Discussion

Multivisceral resections for primary colorectal cancer are extremely complex procedures. One, maybe the most important aspect of these procedures, is a need for the multidisciplinary approach. By doing so, we can expect a good outcome in terms of the morbidity, mortality and favourable oncological result⁷.

There is a number of papers published on this subject, but a direct comparison of results is often difficult. The reason for this is a wide variation of inclusion criteria. In our series, the invasion of neighbouring organs was confirmed by a pathologist in 59.2% of the cases, which was comparable to the majority of other series (malignant invasion in 34% to 58%)¹⁰. An existence of peritumor fibrosis makes a distinction between the adhesions and tumor invasion impossible. In these cases any attempt of division or dissection results in the R1 or R2 resection with the poor outcome. The *en bloc* resection is uniformly advised in order to avoid the tumor cell dissemination and tumor fragmentation^{5-7, 11-13}. The or-

gans/structures most frequently resected in this series were: abdominal wall, urinary bladder and small intestine. This can be explained by the fact that the majority of colon carcinomas were located in the sigmoid colon which is comparable to similar studies^{6, 10, 14, 15}.

An R0 resection, according to the published data is a favourable prognostic factor^{16, 17}. In our study, the R0 resection was achieved in 81.2% which corresponds to the upper range of published data (range 72%–91%)^{14, 15, 18-20}. The R positive resection was, on the other side, associated with the poor prognosis^{9, 19}. Similar conclusion can be reached by looking into our series data, where the patients with the R1 and R2 resection had the poor oncological outcome⁹.

The main limitation of our study, besides its retrospective nature, is the group of patients with rectal cancer. In this group, there was a number of them included in the period when the neoadjuvant treatment was not standardized nor uniformly employed. Hence, the proportion of patients with the neoadjuvant therapy was fairly low, 20.75%. This can explain the relatively high percentage of local recurrence in this group (five-year local recurrence for R0 group was 19.1%), followed by the poor overall and cancer specific survival. The role of neoadjuvant chemoradiotherapy in the local control of rectal cancer is very well known. We can even expect the complete response in the patients planned for the multivisceral resection¹⁴.

Our results confirm that the neoadjuvant therapy is the preferable way to treat the patients with the locally advanced rectal cancer.

In the group of patients with colon cancer, we achieved the results comparable to other studies^{7, 10, 15, 20}.

The five-year local recurrence rate of 26.8% is comparable to the mentioned studies. Adding the absence of neoadjuvant treatment in the rectal cancer group, we can say that these results are acceptable.

In our study, the lymph node involvement was significantly and independently associated with the decreased survival rate. The same conclusion was reached in the studies that emphasized this problem^{6, 20}.

In the context of our results, concerning both patient groups (colon and rectal cancer), we have to stress that a high quality surgery can yield an acceptable oncological outcome even in the absence of appropriate neo and/or adjuvant approach. For this reason, further education and constant improvement of surgical practise should be performed, instead of over-relying on the effect of chemo- and radiotherapy.

Conclusion

We can state that the multivisceral resections have no desired oncological outcome. The results for colon and rectal carcinomas are with no dramatic differences. It is difficult to evaluate properly the oncological outcome of rectal cancer patients, since a small proportion of them received adequate neoadjuvant therapy. We administered this mode of therapy only to the patients with “ugly” carcinomas, most frequently planned for the abdominoperineal amputation. The patients with the node positive disease, or R1 resection had the ex-

tremely poor outcome. Fortunately, a significant proportion of those without the mentioned risk factors had the acceptable outcome. Based on the results and published papers, we can conclude that the meticulous preoperative staging and preoperative therapy both for the colon and rectal patients was the way for further improvement of oncological outcome of multivisceral resections.

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