A META ANALYSIS OF CYTOREDUCTIVE NEPHRECTOMY IN RENAL CELL CARCINOMA.

Vincenzo Di Nunno¹, Lidia Gatto¹, Matteo Santoni², Riccardo Schiavina³, Laura Cosmai⁴, Eugenio Brunocilla³, Andrea Ardizzoni¹, Camillo Porta⁵, Francesco Massari¹

¹Division of Oncology, S. Orsola-Malpighi Hospital, Bologna, Italy; ²Oncology Unit, Macerata Hospital, Macerata Italy; ³Department of Urology, S.Orsola-Malpighi Hospital, Bologna, Italy; ⁴Onco-Nephrology Outpatiients Clinic, San Carlo Borromeo Hospital, ASST Santi Paolo e Carlo, Milan Italy; ⁵ University of Pavia and IRCCS San Matteo University Hospital, Pavia Italy.



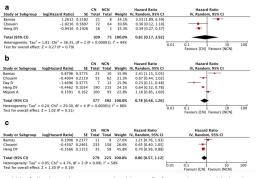
Aim Our aim was to evaluate if performing cytoreductive nephrectomy versus not performing cytoreductive nephrectomy leads to survival benefit in patients with metastatic renal cell carcinoma and in specific subgroups of patients including patients with brain metastases, poor performance status, poor prognosis according to IMDC or MSKCC criteria, clear cell and non-clear cell histologies.

Patients and Methods In our search we identified 16 studies able to provide complete data for the comparison between cytoreductive nephrectomy + systemic treatment vs systemic treatment alone while 9 studies were selected for subgroup analysis. PRISMA guidelines have been adopted to carry out this meta-analysis.

Results: In the overall population, cytoreductive nephrectomy resulted in an OS benefit with a pooled HR of 0.48 (95% CI of 0.42– 0.56) with a significant level of heterogeneity with an I2 value of 92%.

Cytoreductive nephrectomy failed to show a significant survival improvement, with a pooled HR of 0.81 (95%Cl, 0.17–3.92), 0.78 (95% Cl, 0.48–1.26) and 0.80 (95%Cl 0.57–1.12) in patients with brain metastases, poor risk category, and worst performance status, respectively. Cytoreductive nephrectomy resulted in a significant survival improvement in all categories, with a pooled HR of 0.48(95%Cl, 0.38–0.61), 0.47(95%Cl 0.41–0.54), and 0.51 (0.40–0.64) in patients with clear cell RCC, nonclear cell RCC, and papillary RCC, respectively. Heterogeneity was significantly high in the clear cell RCC analysis (I2 = 92%), while moderate levels were observed in non-clear cell RCC (I2 = 57%) and papillary RCC (I2 = 54%).

Cytoreductive Nephrectomy vs No Cytoreductive Nephrectomy in patients with brain metastases, poor prognosis and poor performance status.



We failed to show a survival benefit for patients with brain metastases, a poor risk score according to MSKCC/ IMDC, and poor performance status who underwent to CN. Furthermore, we highlighted a high heterogeneity value for these subgroup analyses. A significant survival improvement in both clear cell RCC, non-clear cell RCC and papillary RCC, has been observed with a moderate level of heterogeneity in both non-clear cell RCC and papillary RCC analyses. In conclusion our study support further investigation of palliative nephrectomy in patients with non clear cell RCC and raise the importance of a better selection of patients which are more likely to benefit from this approach.

References:

- [1] You D et al. J Clin Oncol. 2015;45(1):96–102.
- [2] Motzer RJ et al. N Engl J Med. 2018;379(5):481-2
- [3] Heng DY,, et al. Eur Urol. 2014;66(4):704–10.

			CN	NCN		Hazard Ratio	Hazard Ratio	
Study or Subgroup	log[Hazard Ratio]	SE	Total	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	
Abern MR	-0.9163	0.0383	2629	4514	9.9%	0.40 [0.37, 0.43]		
Aizer AA	-0.6931	0.0806	1998	3057	8.8%	0.50 [0.43, 0.59]	-	
Bamias	-0.6162	0.2993	150	36	3.1%	0.54 [0.30, 0.97]		
Choueiri	-0.3857	0.1955	201	113	5.2%	0.68 [0.46, 1.00]	-	
Conti SL	-0.8916	0.0249	6915	13189	10.2%	0.41 [0.39, 0.43]		
Day D	-0.9416	0.0806	46	45	8.8%	0.39 [0.33, 0.46]	-	
Graham J	-0.478	0.1622	0	0	6.1%	0.62 [0.45, 0.85]	-	
Heng DY	-0.5108	0.07215	982	676	9.1%	0.60 [0.52, 0.69]	-	
Manthieu	-0.6733	0.206	298	53	4.9%	0.51 [0.34, 0.76]		
Marchioni M	-0.9675	0.1145	575	276	7.7%	0.38 [0.30, 0.48]	-	
Tantsugami K	-0.7339	0.2848	254	76	3.3%	0.48 [0.27, 0.84]		
Vaishampayan U	-1.2039	0.03406	7644	4686	10.0%	0.30 [0.28, 0.32]		
Warren M	-0.9675	0.3468	101	33	2.5%	0.38 [0.19, 0.75]		
Xiao WJ	-0.8675	0.1009	1045	460	8.2%	0.42 [0.34, 0.51]	-	
You D	-0.6539	0.4015	96	75	2.0%	0.52 [0.24, 1.14]		
Total (95% CI)			22934	27289	100.0%	0.45 [0.40, 0.51]	•	
Heterogeneity: Tau ² = 0.04: Chi ² = 129.21, df = 14 (P < 0.00001): I ² = 89%								
Test for overall effect	Z = 12.68 (P < 0.00	0.01 0.1 1 10 100 Favours [CN] Favours [NCN]						

Discussion and Conclusion: Overall, our analyses are burdened by a high level of heterogeneity, which reflects the different types of studies included as well as the different temporality and data included. The main weakness of our analysis is the inclusion of retrospective studies due to the scarcity of prospective trials. However, a random effects model was adopted for analysis to account for this. Low risk of biasaccording to NOS (New Ottawa Scale) was calculated in 7 of15 trials, while the others (7/15) presented a moderate risk (forone trial, determination of risk of bias was not performed due to the absence of information about the follow-up period). Considering these limitations, in our analysis, CN resulted in a significant survival benefit.

Cytoreductive Nephrectomy vs No Cytoreductive Nephrectomy in patients with ccRCC, nccRCC, and papillary RCC

а							
				NCN		Hazard Ratio	Hazard Ratio
Study or Subgroup	log[Hazard Ratio]					IV, Random, 95% CI	IV, Random, 95% CI
Abern MR	-1.0216		1619	1147	19.8%	0.36 [0.32, 0.40]	•
Aizer AA	-0.7339			1775	20.1%	0.48 [0.44, 0.53]	•
Day D	-1.5141	0.4425	37	27	5.3%	0.22 [0.09, 0.52]	
Heng DY	-0.6539	0.0691	899	563	19.4%	0.52 [0.45, 0.60]	•
Mèjean A	-0.1165		226	224	17.5%	0.89 [0.72, 1.11]	-
Xiao WJ	-0.8675	0.1009	1045	460	18.0%	0.42 [0.34, 0.51]	•
Total (95% CI)			6495	4196	100.0%	0.48 [0.38, 0.61]	•
Heteropeneity: Tau ² =	0.07: Chi ² = 61.00.	df = 5 (8	< 0.0	0001):	² = 92%		0.01 0.1 1 10 100
Test for overall effect:	Z = 6.22 (P < 0.000	01)					0.01 0.1 1 10 100 Favours [CN] Favours [NCN]
b			CN	NCN		Hazard Ratio	Hazard Batio
Study or Subaroup	log[Hazard Ratio]			Total	Weight	IV. Random, 95% CI	IV. Random, 95% CI
Abern MR	=0.7985		248		32.0%		IV, Kalidoli, JSA Ci
Aizer AA	-0.7985		338		22.4%		
Graham I		0.1622	244		13.2%		· · · · · · · · · · · · · · · · · · ·
Heng DY	-0.4942	0 1681	83	113	12.6%		
Marchioni M	-0.9675		575		19.7%		-
Total (95% CI)			1488	896	100.0%	0.47 [0.41, 0.54]	•
Heterogeneity: Tau ² =			= 0.06	i); 1 ² = !	57%		0.01 0.1 1 10 100
Test for overall effect: Z = 10.28 (P < 0.00001)							Favours [CN] Favours [NCN]
С			CN	NCN		Hazard Ratio	Hazard Ratio
Study or Subgroup	log/Hazard Ratio	I SF			Weight	IV. Random, 95% CI	IV. Random, 95% CI
Aizer AA		0.1191					*
Graham I	-0.475	0.1622	244	109	29.1%		-
Marchioni M	-0.9162	0.1451	387	208	32.5%		
Total (95% CI)			867	479	100.0%	0.51 [0.40, 0.64]	•
Heterogeneity: Tau ²	= 0.02; Chi ² = 4.34,	df = 2 (F	= 0.1	1); 1 ² =	54%		0.01 0.1 1 10 100
Test for overall effect	Z = 5.67 (P < 0.00	001)					0.01 0.1 1 10 100 Favours [CN] Favours [NCN]