Small Primary in Metastatic Disease: Is it Worth to be Removed? CON

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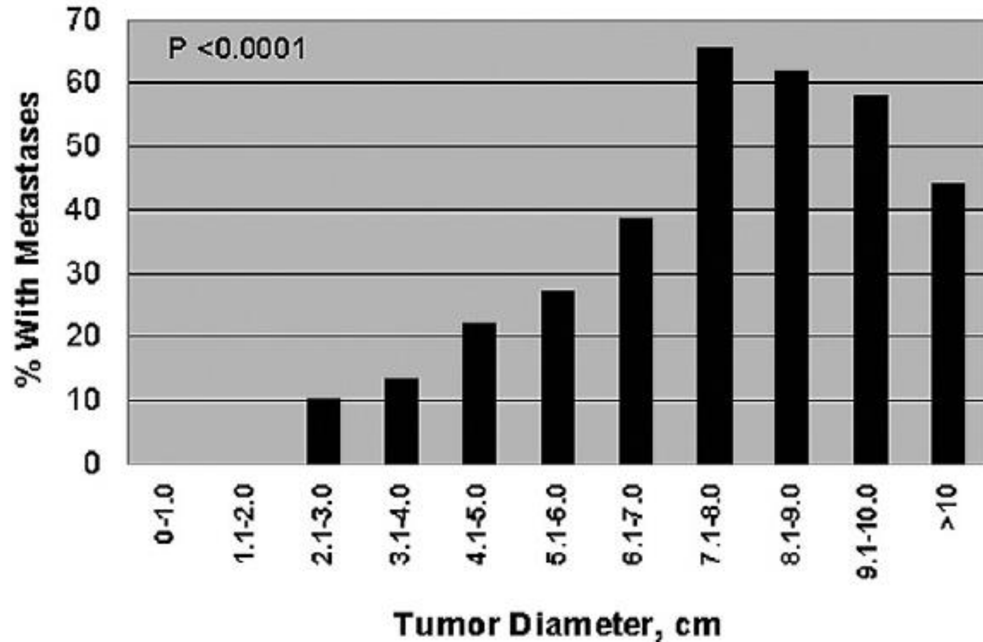
Small primary tumor in mRCC is rare

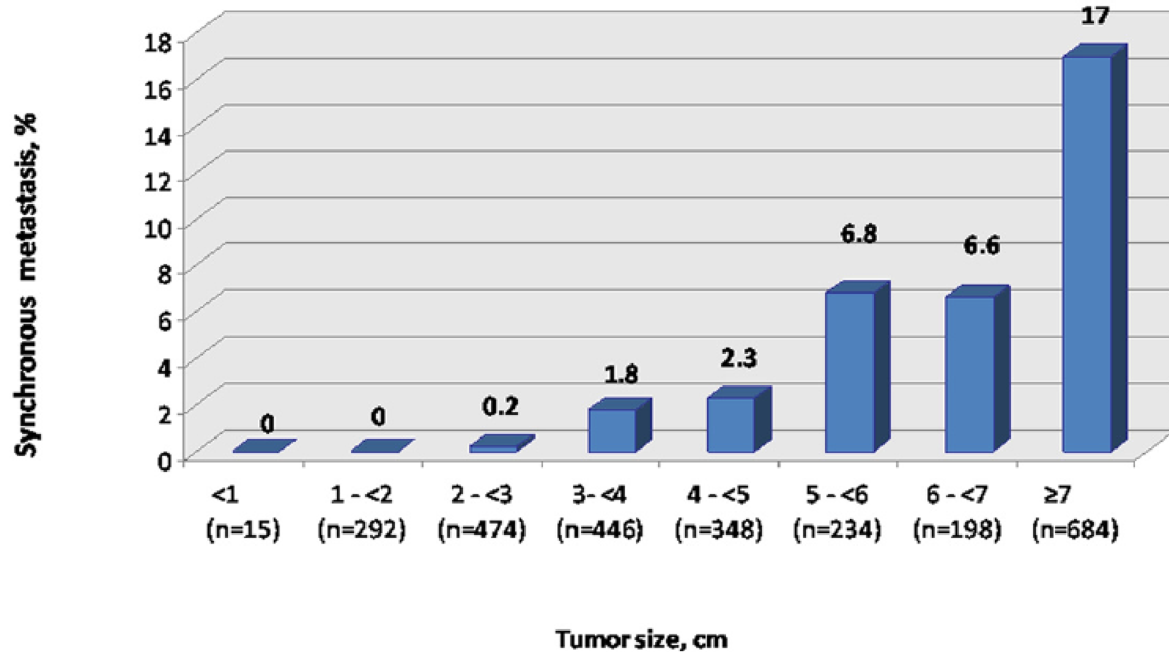
- The probability of synchronous mRCC increased with increasing primary tumor size (p 0.0001).
- no patients with tumors ≤2 cm had confirmed metastatic disease
- <5% of all synchronous metastasis occurred in tumors ≤ 3.0 cm
- the odds of synchronous metastasis increased by 22% for each 1 cm increase in tumor size.



Kunkle DA et al., J Urol, 2007

Small primary tumor in mRCC is rare

- 0.2% patients with a tumor <3 cm had mRCC
- 2% of T1a tumors had mRCC
- tumor size was significantly associated with metastasis at presentation
  - for each 1 cm increase OR 1.25, p 0.001.



Kunkle DA et al., J Urol, 2007

Characteristics of SRT

- Small primary tumors are usually asymptomatic
- Growth rate or small renal masses is low
  - These features are not in favour of upfront nephrectomy in mRCC
- If we perform a nephrectomy, it means that we are convinced that primary tumor resection will improve survival

Volpe et al. Eur Urol 2011

Prognostication in mRCC

	Database Consortium model[7]	CCF model[9]	French model[10,11]	IKCWG model[12]*	MSKCC model[13]
Risk factors					
Karnofsky performance status or ECOG PS	✓	✓	✓	✓	✓
Time from diagnosis to treatment	✓	✓	..	✓	✓
Time from diagnosis to metastasis	..	..	✓	..	..
Number of metastatic sites	..	..	✓	✓	..
Liver metastasis	..	..	✓	..	..
Previous immunotherapy	..	..	..	✓	..
Haemoglobin concentration	✓	..	..	✓	✓
Corrected or uncorrected calcium concentration	✓	✓	..	✓	✓
Neutrophil count	✓	✓	..	..	..
Platelet count	✓	✓	..	..	..
Lactate dehydrogenase concentration	..	..	..	✓	✓
White blood cell count	..	..	..	✓	..
Alkaline phosphatase concentration	..	..	..	✓	..

Tumor size of the primary tumor is not a prognostic factor in mRCC

The Impact of Tumor Burden Characteristics in Patients With Metastatic Renal Cell Carcinoma Treated With Sunitinib

Naveen S Basappa, MD[1]; Paul Elson, ScD[1]; Ali-Reza Golshayan, MD[2]; Laura Wood, RN[1]; Jorge A Garcia, MD[1]; Robert Dreicer, MD[1]; and Brian I Rini, MD[1]

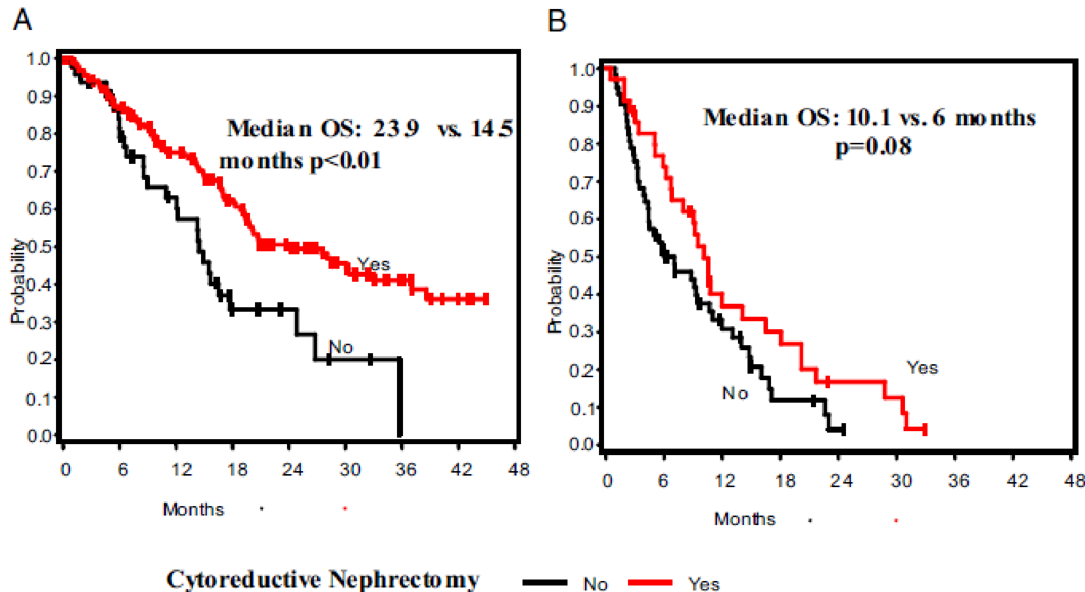
- In case of small primary tumor, it is likely that tumor burdern witch will drive prognostic and survival
- Is outside of the kidney

Basappa et al., Cancer, 2011

Therefore, Removing Small Primary Tumor →Is even more Debatable than removing kidney in Metastatic Disease

Uncertainty on the role of nephrectomy in mRCC; Data from retrospective study

The Impact of Cytoreductive Nephrectomy on Survival of Patients With Metastatic Renal Cell Carcinoma Receiving Vascular Endothelial Growth Factor Targeted Therapy



Choueiri et al., J Urol 2011

Uncertainty on the role of nephrectomy in mRCC

Phase 3 Randomized Study Comparing Nephrectomy Plus Sunitinib vs Sunitinib Without Nephrectomy in First-Line Metastatic RCC

Carmena trial

RANDOMIZATION

Nephrectomy → **Sunitinib 50 mg 4/2**

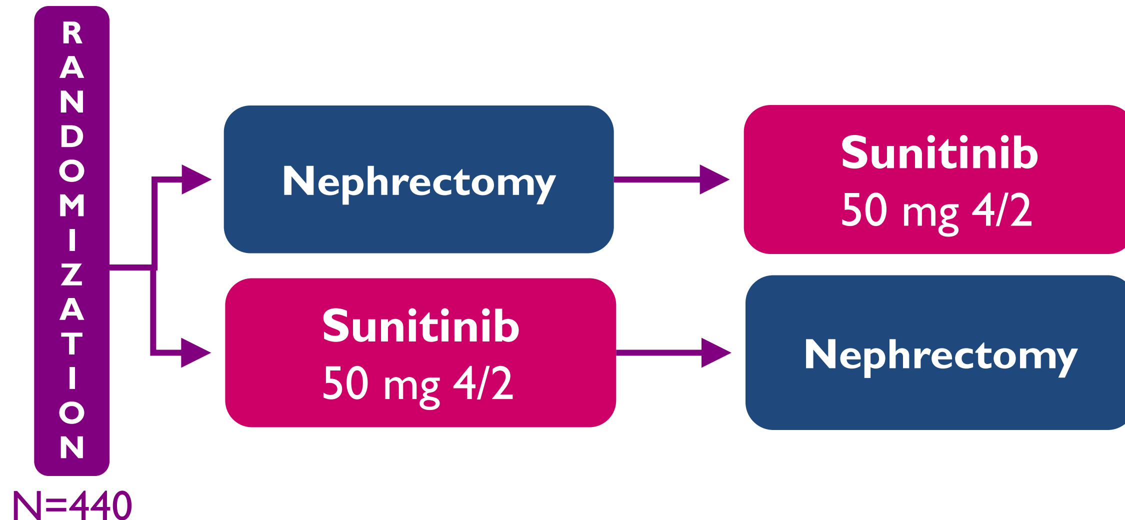
Sunitinib 50 mg 4/2

N=576

CARMENA Study, PI: Pr Arnaud Mejean (CCAFU – HEGP Hospital – Paris, France)

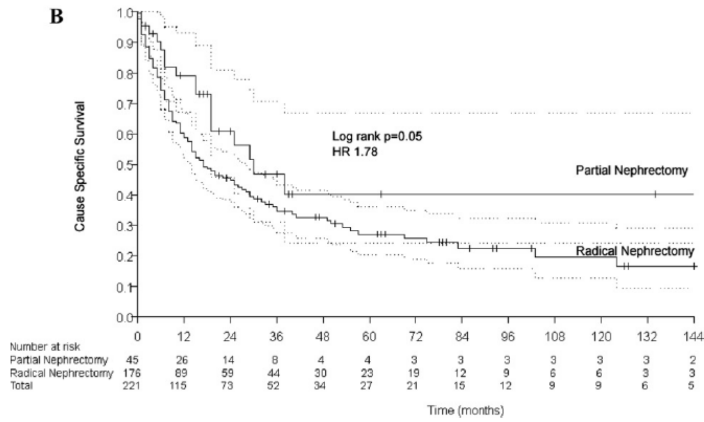
Uncertainty on the role of nephrectomy in mRCC

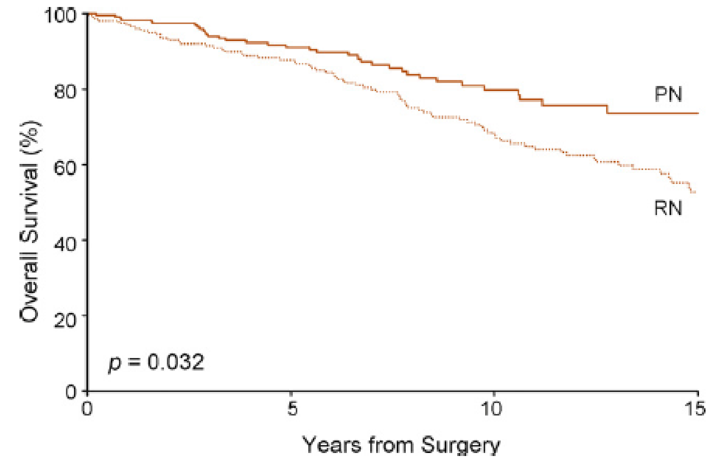
Sunitinib Followed by Nephrectomy in Case of Non-Progressive Metastases Followed by Sunitinib vs Nephrectomy Followed by Sunitinib in Patients With Synchronous Metastatic Renal Cell Carcinoma and the Primary Tumor in Situ



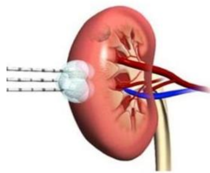
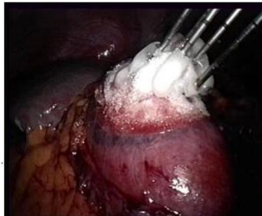
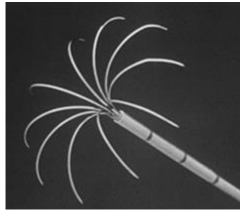
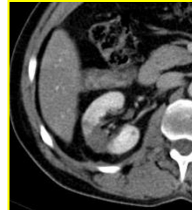
PI: Pr Axel Bex – Netherlands – EORTCGU Group Study

No place for radical nephrectomy





Ablative Treatments are alternative approaches: RFA, Cryo Ablation

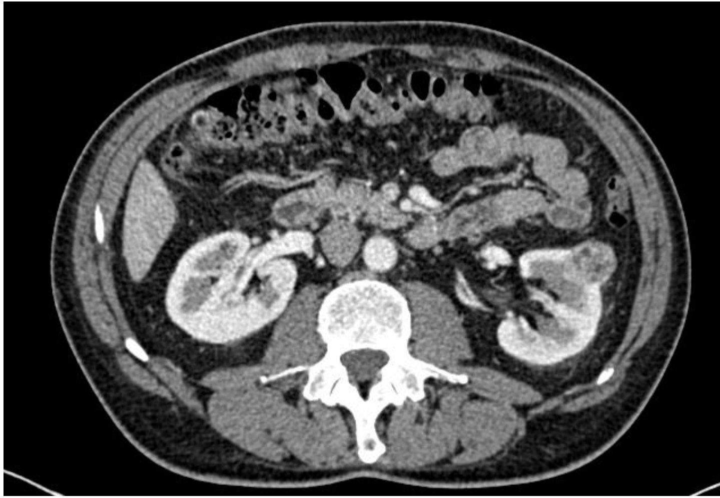





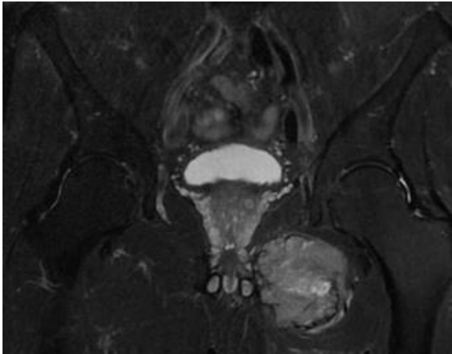
Capitanio et al., Urology, 2008
Kaushik et al., Eur Urol, 2012
Psutka et al., Eur Urol, 2013

Scenarios for small primary tumor resection

- Small primary Tumor and low distant tumor burden (infra centri metric pulmonary nodules)→ PN followed by surveillance, systemic treatment in case of progression
- Small primary Tumor and resectable distant metastases→ resection of all tumors and close follow-up until progression
- Rapidly growing renal tumor while other sites are stable under systemic treatment
- Complete response for distant mets and persistant renal tumor→ PN

The case for PN in small primary Renal tumor: solitary bone met + SRT





Conclusions

- Upfront nephrectomy in case of small primary mRCC should not be considered as a standard of care.
- In rare cases where primary tumor treatment is needed we should favor
  - Nephron sparing approaches
  - mini invasive approaches (robot PN, Ablative treatment)
- We should encourage, inclusion into clinical trials