KEY QUESTION 1

1. KEY QUESTION 1

a. Wat is de meerwaarde van lokale behandeling, al dan niet gecombineerd met neoadjuvante (chemo)radiotherapie, ten opzichte van conventionele chirurgie bij patiënten met een stadium 1-4 rectumcarcinoom op het gebied van lokale controle, Qol en OS?

P: patiënten met een stadium stadium 1-4 rectumcarcinoom

I: lokale behandeling (chirurgische excisies van volledige dikte van de rectumwand: *transanal excision using a retractor (Parks), transanal endoscopic microsurgery (TEM), single port transanal endoscopic surgery (SPTS): niet:* Endoscopic Mucosal Resection (EMR)) + neoadjuvante (chemo)radiotherapie

C: conventionele (Total Mesorectal Excision, Abdomino Perineal Resection) chirurgie, al dan niet met neo-adjuvante (chemo)radiotherapie

O: lokale controle, OS, QoL

2. SEARCH STRATEGY 1

Searches were run on December 2012 for systematic reviews (SRs), randomised controlled trials (RCTs) and observational studies. Pubmed Medline, OVID Embase and the Cochrane Database of Systematic Reviews (CDSR) were searched. Detailed search strings are given below.

3. SEARCH RESULTS 1

SYSTEMATIC REVIEWS AND META-ANALYSES

The Medline search yielded 24 hits, while the Embase search yielded 349 hits. The search in the CDSR yielded no Cochrane reviews.

FULL-TEXT EVALUATION

After merging the 2 search files into 1 file and removal of the duplicates, 326 records were screened on title and abstract. Of these 311 were excluded. The most important reasons for exclusion were that studies were on other patients, interventions or comparisons.

Of the remaining 15 studies, the full-text was retrieved. In addition, 1 file was found through reference tacking. Table 1 provides an overview of the evaluation of these 16 studies.

Table 1. Key question 1: overview of reviews evaluated full-text.

| | Reference | In- /Excluded | Reason(s) |
|---|---|------------------|---|
| 1 | Barendse, R. M., F. J. C. Van Den Broek, et al. (2011). "Systematic review of endoscopic mucosal resection versus transanal endoscopic microsurgery for large rectal adenomas." <u>Endoscopy</u> 43 (11): 941-949 | Ex | On rectal adenomas |
| | Borschitz, T., D. Wachtlin, et al. (2008). "Neoadjuvant chemoradiation and local excision for T2-3 rectal cancer." Annals of surgical oncology 15(3): 712-720. | Ex | No quality appraisal, used for reference tracking |
| | Carrara, A., D. Mangiola, et al. (2011). "Local excision | Ex | Review in abstract form |

| | Reference | In- /Excluded | Reason(s) |
|----|---|------------------|--|
| | as single treatment for early stages of rectal cancer: Indications and causes of local failure. Systematic literature review and meta- analysis." <u>Techniques in</u> <u>Coloproctology</u> 15 (2) : 235. | | |
| | Doornebosch, P. G., R. A. Tollenaar, et al. (2009). "Is the increasing role of Transanal Endoscopic Microsurgery in curation for T1 rectal cancer justified? A systematic review." <u>Acta Oncol</u> 48 (3): 343-353 | Ex | No quality appraisal, unclear whether patients in included studies had had neoadjuvant (chemo)radiation |
| 5 | Hingorani, M., J. E. Hartley, et al. (2012). "Avoiding radical surgery after pre- operative chemoradiotherapy: A possible therapeutic option in rectal cancer?" <u>Acta Oncologica</u> 51 (3): 275-284 | Ex | No quality appraisal, used for reference tracking |
| | Martin, S. T., H. M. Heneghan, et al. (2012). "Systematic review and meta- Analysis of outcomes following pathological complete response to neoadjuvant chemoradiotherapy for rectal cancer." <u>British Journal of Surgery</u> 99 (7): 918-928 | Ex | >98% of patients included in included series did not have a local excision; the meta- analyses excluded those patients |
| | Martin, S. T., H. M. Heneghan, et al. (2012). "Systematic review of outcomes after intersphincteric resection for low rectal cancer." <u>British Journal of</u> <u>Surgery</u> 99 (5): 603-612 | Ex | On intersphincteric resection |
| | Praveen, C. R. (2011). "Transanal endoscopic microsurgery: Where it stands as of today?" <u>World</u> Journal of Laparoscopic Surgery 4 (2): 109-115 | Ex | No quality appraisal |
| | Repici, A., C. Hassan, et al. (2012). "Efficacy and safety of endoscopic submucosal dissection for colorectal neoplasia: a systematic review." Endoscopy 44 (2): 137-150 | Ex | On endoscopic submucosal resection |
| 10 | Sgourakis, G., S. Lanitis, et al. (2011). "Transanal endoscopic microsurgery for T1 and T2 rectal cancers: a meta- analysis and meta- regression analysis of outcomes." <u>Am Surg</u> 77 (6): 761-772 | Ex | Only one out of 11 included studies used neoadjuvant therapy. Used for reference tracking |
| | Smith, F. M., D. Waldron, et al. (2010). "Rectum- conserving surgery in the era of chemoradiotherapy." British Journal of Surgery 97 (12): 1752-1764 | Ex | No quality appraisal, used for reference tracking |
| | Suppiah, A., S. Maslekar, et al. (2008). "Transanal endoscopic microsurgery in early rectal cancer: time for a trial?" <u>Colorectal Dis</u> 10 (4): 314-327; discussion 327-319 | Ex | No quality appraisal, used for reference tracking |
| | Tappenden, P., J. Chilcott, et al. (2009). "Systematic review of economic evidence for the detection, diagnosis, treatment, and follow- up of colorectal cancer in the United Kingdom." <u>International journal</u> of technology assessment in health care 25 (4): 470- 478 | Ex | No studies on local therapy included |
| | Taylor, I. (2008). "Surgical issues in rectal cancer." Annals of Oncology 19 (58) : viii41- viii42. | Ex | Narrative review |
| 15 | Tytherleigh, M. G., B. F. Warren, et al. (2008). "Management of early rectal cancer." <u>British Journal</u> of Surgery 95 (4): 409-423 | Ex | Narrative review based on a systematic search |
| 16 | Wu, Y., Y. Y. Wu, et al. (2011). "TEM and conventional rectal surgery for T1 rectal cancer: A meta- analysis." <u>Hepato- Gastroenterology</u> 58 (106): 364-368 | Ex | No quality appraisal, used for reference tracking |

OTHER STUDIES

The Medline search yielded 1122 hits, while the Embase search yielded 2399 hits.

FULL-TEXT EVALUATION

After merging the 2 search files into 1 file and removal of the duplicates, 3086 hits were screened on title and abstract. Of these, 2881 were excluded. The most important reasons for exclusion were that studies were concerned with other patients or other interventions.

Of the remaining 205 studies, the full-text was retrieved. Table 2 provides an overview of the evaluation of these studies. In addition, 15 studies were identified through reference tracking and evaluated full text (table 3).

Studies had to include at least X patients whom had received neoadjuvant therapy. The follow-up should be at least 1 year.

Table 2. Key question 1: overview of full-text evaluated other studies

| | Reference | In- /Excluded | Reason(s) |
|----|--|------------------|---|
| 1 | Allaix, M. E., A. Arezzo, et al. (2012). "Transanal Endoscopic Microsurgery for Rectal Neoplasms. How I Do It." J Gastrointest Surg. | Ex | Describes oncologic outcomes of a series included for full text selection (Morino 2011) |
| | Allaix, M. E., A. Arezzo, et al. (2009). "Transanal endoscopic microsurgery for rectal neoplasms: experience of 300 consecutive cases." <u>Dis Colon Rectum</u> 52 (11): 1831-1836. | Ex | T1 series (38 patients without neoadjuvant therapy); T2 and T3 patients: only 3/37 T2 patients received neoadjuvant therapy |
| | Allaix, M. E., A. Arezzo, et al. (2011). "Risk factors for recurrence after transanal endoscopic microsurgery for rectal malignant neoplasm." <u>Surgical Endoscopy and Other</u> <u>Interventional Techniques</u> 25 : S28. | Ex | Neoadjuvant treatment for T1 not mentioned. 'Five patients with pT2 cancer who received a neo-adjuvant treatment are disease-free, while recurrence occurred in 26.3% (10/38) pT2 cancers submitted either to surgery, adjuvant therapy or to clinical surveillance. Recurrence rate in pT3 was 46%' |
| | Allaix, M. E., A. Arezzo, et al. (2012). "Transanal endoscopic microsurgery versus laparoscopic total mesorectal excision for selected T2N0 rectal cancer." <u>Digestive and Liver Disease</u> 44 : S169. | Ex | 11 of 43 P2 patients were treated neoadjuvantly. Observational study |
| | Allaix, M. E., A. Arezzo, et al. (2012). "Transanal Endoscopic Microsurgery vs. Laparoscopic Total Mesorectal Excision for T2N0 Rectal Cancer." <u>J Gastrointest Surg</u> 16 (12): 2280-2287. | Ex | 43 T2N0 TEM patients, 11 of whom received neoadjuvant RT. Observational study |
| | Allaix, M. E., A. Arezzo, et al. (2011). "Transanal endoscopic microsurgery versus laparoscopic total mesorectal excision for selected T2N0 rectal cancer." <u>Techniques in</u> <u>Coloproctology</u> 15 (2) : 235-236. | | On request |
| | Allaix, M. E., M. Mistrangelo, et al. (2009). "Transanal endoscopic microsurgery for rectal malignant neoplasms. Results of IO4 consecutive patients." <u>Colorectal Disease</u> 11 : 50. | Ex | Neoadjuvant therapy not mentioned for T1 or T3 patients |
| | Allaix, M. E., F. Rebecchi, et al. (2011). "Long-term functional results and quality of life after transanal endoscopic microsurgery." <u>Br J Surg</u> 98 (11): 1635-1643. | Ex | Outcomes not reported separately for benign and malign disease |
| | Amann, M., A. Modabber, et al. (2012). "Transanal endoscopic microsurgery in treatment of rectal adenomas and T1 low-risk carcinomas." <u>World J Surg Oncol</u> 10 (1): 255. | Ex | 41 T1 carcinomas, no mention of neoadjuvant therapy |
| 10 | Araujo, S. E., V. E. Seid, et al. (2012). "Transanal endoscopic microsurgery: a Brazilian initial experience in private practice." <u>Hepatogastroenterology</u> 59 (118): 1822-1827. | | On request |
| | Arezzo, A., M. E. Allaix, et al. (2010). "Risk factors for recurrence after transanal endoscopic microsurgery for rectal malignant neoplasm." <u>Colorectal Disease</u> 12 : 3. | Ex | Neoadjuvant therapy not mentioned |
| | Ashraf, S., R. Hompes, et al. (2012). "A critical appraisal of endorectal ultrasound and transanal endoscopic microsurgery and decision-making in early rectal cancer." <u>Colorectal Dis</u> 14(7): 821-826. | Ex | Other focus |
| | Atallah, S., M. Albert, et al. (2010). "Transanal minimally invasive surgery: a giant leap forward." <u>Surg Endosc</u> 24(9): | Ex | Sort follow-up (6 weeks) |

| | Reference | In- /Excluded | Reason(s) |
|----|---|------------------|--|
| | 2200-2205. | | |
| | Baatrup, G., B. Breum, et al. (2009). "Transanal endoscopic microsurgery in 143 consecutive patients with rectal adenocarcinoma: results from a Danish multicenter study." <u>Colorectal Dis</u> 11 (3): 270-275. | Ex | In: 72 T1 patients; Ex: T2 and T3 patients: neoadjuvant therapy not mentioned |
| 15 | Bach, S. P., J. Hill, et al. (2009). "A predictive model for local recurrence after transanal endoscopic microsurgery for rectal cancer." <u>Br J Surg</u> 96 (3): 280-290. | Ex | '39 received neoadjuvant long-course radiotherapy and were excluded from the main analysis owing to the possibility of stage migration' |
| | Badiani, S., M. Peacock, et al. (2012). "Organ preservation is possible: Local excision of early rectal cancer with Transanal Endoscopic Microsurgery (TEMS)." <u>Colorectal Disease</u> 14: 16. | In | 9 T1 patients treated neoadjuvantly; 3 T3 patients treated neoadjuvantly |
| | Badiani, S., M. Peacock, et al. (2012). "TEMS as treatment for early rectal cancer: A single regional referral centre experience." <u>Colorectal Disease</u> 14 : 19-20. | | On request |
| | Bansal, V. K., M. C. Misra, et al. (2010). "Transanal excision of anorectal lesions." <u>Trop Gastroenterol</u> 31 (1): 1-4. | | On request |
| | Barendse, R. M., P. G. Doornebosch, et al. (2012). "Transanal employment of single access ports is feasible for rectal surgery." <u>Ann Surg</u> 256 (6): 1030-1033. | Ex | No long-term follow-up |
| 20 | Barendse, R. M., P. Fockens, et al. (2011). "The significant rectal neoplasm and mucosectomy by transanal endoscopic microsurgery (Br J Surg 2011; 98: 1342-1344)." <u>Br J Surg</u> 98 (10): 1495; author reply 1495-1496. | Ex | Letter with no original observational data |
| | Barendse, R. M., F. J. van den Broek, et al. (2012). "Endoscopic mucosal resection vs transanal endoscopic microsurgery for the treatment of large rectal adenomas." <u>Colorectal Dis</u> 14(4): e191-196. | Ex | On rectal adenomas |
| | Barker, J. A. and J. Hill (2011). "Incidence, treatment and outcome of rectal stenosis following transanal endoscopic microsurgery." <u>Tech Coloproctol</u> 15 (3): 281-284. | Ex | Other outcome: rectal stenosis |
| | Barreto, S. G. and P. J. Shukla (2008). "Local excision and endoscopic posterior mesorectal resection versus low anterior resection in T1 rectal cancer (Br J Surg 2008; 95: 375- 380)." <u>British Journal of Surgery</u> 95 (7): 930-931. | Ex | 18 T1 patients; neoadjuvant treatment not mentioned |
| | Beets, G. L., L. A. Heijnen, et al. (2012). "Minimal invasive treatment for clinical complete and good responders after chemoradiation for rectal cancer." <u>European Journal of Surgical Oncology</u> 38 (9): 755. | Ex | Little information on 5 TEM patients |
| | Belluco, C., A. De Paoli, et al. (2011). "Long-term outcome analysis of patients with complete pathological response after neoadjuvant chemoradiation for cT3 rectal cancer: Implications for local excision surgical strategies." <u>Annals of</u> <u>Surgical Oncology</u> 18 : S30. | Ex | Abstract of which the full article is included for full text evaluation (Belluco 2011) |
| | Belluco, C., A. De Paoli, et al. (2011). "Long-term outcome of patients with complete pathologic response after neoadjuvant chemoradiation for cT3 rectal cancer: implications for local excision surgical strategies." <u>Ann Surg</u> <u>Oncol</u> 18 (13): 3686-3693. | In | 29 cT3 patients treated by local excision after neoadjuvant chemoradiotherapy |
| | Belluco, C., A. De Paoli, et al. (2010). "Long-term results using local excision after neoadjuvant chemoradiation therapy in T3 rectal cancer patients." <u>European Journal of Surgical</u> <u>Oncology</u> 36 (9) : 884. | Ex | Abstract of which the full article is included for full text evaluation (Belluco 2011) |
| | Bertrand, M., P. Rouanet, et al. (2012). "TransAnal Endoscopic Proctectomy (TAEP) e An innovative procedure for difficult resection of rectal tumors in men with narrow pelvis." <u>European Journal of Surgical Oncology</u> 38 (9) : 755-756. | | On request |
| | Bignell, M. B., A. Ramwell, et al. (2010). "Complications of transanal endoscopic microsurgery (TEMS): a prospective audit." <u>Colorectal Dis</u> 12 (7 Online): e99-103. | Ex | Sort follow-up |

| | Reference | ln- /Excluded | Reason(s) |
|----|--|------------------|--|
| 30 | Bokkerink, G. M., E. J. de Graaf, et al. (2011). "The CARTS study: Chemoradiation therapy for rectal cancer in the distal | Ex | Study protocol |
| | rectum followed by organ-sparing transanal endoscopic | | |
| | microsurgery." <u>BMC Surg</u> 11 : 34. Bokkerink, G. M. J., I. H. J. T. De Hingh, et al. (2011). | Ex | Short follow-up |
| | "Transanal endoscopic microsurgery (TEM) after | | |
| | (Chemo)radiation therapy for distal rectal cancer." European | | |
| | Journal of Cancer 47: S402. | | - |
| | Borley, N. (2011). "Long-term functional results and quality of | | On request |
| | life after transanal endoscopic microsurgery (Br J Surg 2011; 98: 1635-1643)." <u>Br J Surg</u> 98 (11): 1635-1643. | | |
| | Borley, N. (2012). "Transanal glove port is a safe and cost- effective alternative for transanal endoscopic microsurgery | | On request |
| | (Br J Surg 2012; 99: 1429-1435)." <u>Br J Surg</u> 99 (10): 1435. | | |
| | Borley, N. R. and J. M. Wheeler (2011). "The significant rectal | Ex | Expert opinion-type article |
| | neoplasm and mucosectomy by transanal endoscopic | | |
| | microsurgery." <u>Br J Surg</u> 98(10): 1342-1344. | | |
| | Borschitz, T., I. Gockel, et al. (2008). "Oncological outcome | Ex | Neoadjuvant therapy not mentioned |
| | after local excision of rectal carcinomas." <u>Ann Surg Oncol</u> | | |
| | 15 (11): 3101-3108. | Ev | Narrative review, used for reference |
| | Borschitz, T., W. Kneist, et al. (2008). "Local excision for more advanced rectal tumors." <u>Acta Oncol</u> 47 (6): 1140-1147. | Ex | Narrative review, used for reference tracking |
| | Borschitz, T., D. Wachtlin, et al. (2008). "Neoadjuvant | Ex | Narrative review, used for reference |
| | chemoradiation and local excision for T2-3 rectal cancer." | | tracking |
| | <u>Ann Surg Oncol</u> 15 (3): 712-720. | | |
| | Brenner, B., R. Brenner, et al. (2010). "Local excision after | | On request |
| | neoadjuvant chemoradiation for rectal cancer: Is it an | | |
| | acceptable treatment option?" Journal of Clinical Oncology. | | |
| | <u>Conference</u> 28 (15 SUPPL. 1). Bujko, K., P. Richter, et al. (2009). "Preoperative radiotherapy | In | 47 T1-2 patients treated with neoadjuvant |
| | and local excision of rectal cancer with immediate radical re- | | therapy |
| | operation for poor responders." <u>Radiother Oncol</u> 92(2): 195-201. | | |
| 40 | Bujko, K., P. Richter, et al. (2011). "Preoperative radiotherapy | Ex | 89 T1-T3 patients treated neoadjuvantly. |
| | and local excision of rectal cancer: Results of a randomized | | Results not presented per stage |
| | study." <u>Radiotherapy and Oncology</u> 99: S64. | _ | |
| | Burger, J. W., E. J. de Graaf, et al. (2010). "Local excision of | Ex | Description of a single case |
| | rectal cancer after chemoradiation: feasibility depends on the primary stage." Int J Colorectal Dis 25 (9): 1141-1142. | | |
| | Callender, G. G., P. Das, et al. (2010). "Local excision after | In | 47 T3 patients treated with local excision |
| | preoperative chemoradiation results in an equivalent | | after neoadjuvant chemoradiation |
| | outcome to total mesorectal excision in selected patients | | |
| | with T3 rectal cancer." <u>Ann Surg Oncol</u> 17 (2): 441-447. | | |
| | Camp, E. R., J. T. Lucas, et al. (2011). "Local excision and | | On request |
| | selective radical resection after neoadjuvant chemoradiation | | |
| | for rectal cancer." <u>Journal of Clinical Oncology. Conference:</u> <u>ASCO Annual Meeting</u> 29 (15 SUPPL. 1). | | |
| | Canda, A. E., C. Terzi, et al. (2012). "Transanal single-port | Ex | Adenomas and 1 carcinoma in situ |
| | access microsurgery (TSPAM)." Surg Laparosc Endosc | | |
| | <u>Percutan Tech</u> 22 (4): 349-353. | | |
| | Carmichael, J. C. and M. J. Stamos (2011). "Ransanal excision | | On request |
| | of rectal cancer: A work in progress." <u>Oncology</u> 25 (14). | _ | |
| | Carrara, A., D. Mangiola, et al. (2011). "Local excision as | Ex | Review in abstract form |
| | single treatment for early stages of rectal cancer: Indications | | |
| | and causes of local failure. Systematic literature review and meta-analysis." <u>Techniques in Coloproctology</u> 15 (2) : 235. | | |
| | Carroll, P. A., J. Larkin, et al. (2012). "T1 colorectal cancers: | | On request |
| | How appropriate is local excision?" <u>Colorectal Disease</u> 14: 17. | | |
| | Cattorini, L., M. Coccetta, et al. (2009). "PT2 report after | | On request |
| | transanal endoscopic microsurgery excision in elderly patient | | |

| | Reference | In- /Excluded | Reason(s) |
|----|--|------------------|---|
| | T1 staged: A case report." <u>BMC Geriatrics</u> 9(SUPPL. 1). | | |
| | Chang, A. J., C. S. Nahas, et al. (2008). "Early rectal cancer: local excision or radical surgery?" <u>J Surg Educ</u> 65 (1): 67-72. | Ex | Narrative review |
| 50 | Chen, Y. Y., Z. H. Liu, et al. (2012). "Transanal Endoscopic Microsurgery versus Laparoscopic Lower Anterior Resection for the Treatment of T1-2 Rectal Cancers." <u>Hepatogastroenterology</u> 60 (124). | | On request |
| | Christoforidis, D., H. M. Cho, et al. (2009). "Transanal endoscopic microsurgery versus conventional transanal excision for patients with early rectal cancer." <u>Ann Surg</u> 249 (5): 776-782. | Ex | Patients with neoadjuvant therapy were excluded |
| | Clark, J. and P. Ziprin (2008). "Local excision and transanal endoscopic microsurgery in the management of rectal cancer with a focus on early carcinoma." <u>Future Oncol</u> 4 (1): 113-124. | | On request |
| | Collinson, R. J. and C. M. N. J. Mc (2009). "'How i do it': TEM for tumors of the rectum." <u>Journal of Gastrointestinal Surgery</u> 13 (2): 359-362. | Ex | Not an observational study |
| | Dalton, S. J., O. J. Old, et al. (2010). "The management of early rectal cancer with transanal endoscopic microsurgery: Our experience." <u>Colorectal Disease</u> 12 : 20-21. | | On request |
| | Darwood, R. J., J. M. Wheeler, et al. (2008). "Transanal endoscopic microsurgery is a safe and reliable technique even for complex rectal lesions." <u>Br J Surg</u> 95 (7): 915-918. | Ex | Includes complex rectal lesions only |
| | De Graaf, E. J., P. G. Doornebosch, et al. (2009). "Transanal endoscopic microsurgery versus total mesorectal excision of T1 rectal adenocarcinomas with curative intention." <u>Eur J</u> <u>Surg Oncol</u> 35 (12): 1280-1285. | Ex | Same patients as Doornebosch 2010 |
| | Doornebosch, P. G., F. T. Ferenschild, et al. (2010). "Treatment of recurrence after transanal endoscopic microsurgery (TEM) for T1 rectal cancer." <u>Dis Colon Rectum</u> 53 (9): 1234-1239. | Ex | 88 T1 patients; neoadjuvant therapy not mentioned |
| | Doornebosch, P. G., M. P. Gosselink, et al. (2008). "Impact of transanal endoscopic microsurgery on functional outcome and quality of life." Int J Colorectal Dis 23 (7): 709-713. | Ex | Series of 47 patients out of whom 44 had an adenoma |
| | Doornebosch, P. G., R. A. Tollenaar, et al. (2009). "Is the increasing role of Transanal Endoscopic Microsurgery in curation for T1 rectal cancer justified? A systematic review." <u>Acta Oncol</u> 48 (3): 343-353. | Ex | Review, no quality appraisal |
| 60 | Doornebosch, P. G., E. Zeestraten, et al. (2012). "Transanal endoscopic microsurgery for T1 rectal cancer: size matters!" <u>Surg Endosc</u> 26 (2): 551-557. | Ex | Other outcome: risk factors for recurrence, in a series that has been included (Doornebosch 2010) |
| | Druzijanic, N., Z. Perko, et al. (2008). "Harmonic scalpel in transanal microsurgery." <u>Hepatogastroenterology</u> 55 (82-83): 356-358. | | On request |
| | Duek, S. D., N. Issa, et al. (2008). "Outcome of transanal endoscopic microsurgery and adjuvant radiotherapy in patients with T2 rectal cancer." <u>Dis Colon Rectum</u> 51 (4): 379-384; discussion 384. | Ex | T2 patients without neoadjuvant therapy |
| | Dumont, F., D. Goere, et al. (2012). "Transanal endoscopic total mesorectal excision combined with single-port laparoscopy." <u>Dis Colon Rectum</u> 55 (9): 996-1001. | Ex | Short follow-up |
| | Fantola, G., L. Zorcolo, et al. (2010). "Transanal endoscopic microsurgical excision - A valid treatment for early rectal cancer." <u>European Journal of Surgical Oncology</u> 36 (9) : 883. | Ex | 26 T1 patients, neoadjuvant therapy not mentioned |
| | Folkesson, J. and L. Pahlman (2008). "Authors' reply: Population-based study of local surgery for rectal cancer (Br J Surg 2007; 94: 1421-1426)." <u>British Journal of Surgery</u> 95 (2): 262. | Ex | Author's reply with no additional data |
| | Friel, C. M. (2010). "Local excision of T1 rectal cancer: where are we now?" <u>Dis Colon Rectum</u> 53 (9): 1231-1233. | Ex | Editorial |

| | Reference | In- /Excluded | Reason(s) |
|----|---|------------------|--|
| | Funahashi, K., J. Koike, et al. (2009). "Transanal rectal dissection: a procedure to assist achievement of laparoscopic total mesorectal excision for bulky tumor in the narrow pelvis." <u>Am J Surg</u> 197 (4): e46-50. | Ex | On TME |
| | Garcia-Aguilar, J., Q. Shi, et al. (2010). "Pathologic complete response (pCR) to neoadjuvant chemoradiation (CRT) of uT2uN0 rectal cancer (RC) treated by local excision (LE): Results of the ACOSOG Z6041 trial." <u>Journal of Clinical</u> <u>Oncology. Conference</u> 28 (15 SUPPL. 1). | Ex | Editorial |
| | Garcia-Aguilar, J., Q. Shi, et al. (2012). "A phase II trial of neoadjuvant chemoradiation and local excision for T2N0 rectal cancer: preliminary results of the ACOSOG Z6041 trial." <u>Ann Surg Oncol 19(2)</u> : 384-391. | Ex | Only peri-procedural outcomes reported |
| 70 | Garcia-Aguilar, J. (2013). "Transanal endoscopic microsurgery following neoadjuvant chemoradiation therapy in rectal cancer: a word of caution about patient selection?" <u>Dis Colon</u> <u>Rectum</u> 56 (1): 1-3 | | On request |
| | Gleeson, F. C., J. E. Clain, et al. (2011). "Surveillance EUS FNA following transanal excision of primary rectal cancer facilitates early detection of local recurrence." <u>Gastrointestinal Endoscopy</u> 1): AB170. | Ex | Other focus |
| | Gleeson, F. C., D. W. Larson, et al. (2012). "Local recurrence detection following transanal excision facilitated by EUS-FNA." <u>Hepatogastroenterology</u> 59 (116): 1102-1107. | | On request |
| | Greenberg, J. A., D. Shibata, et al. (2008). "Local excision of distal rectal cancer: an update of cancer and leukemia group B 8984." <u>Dis Colon Rectum</u> 51 (8): 1185-1191; discussion 1191-1184. | Ex | In: 59 T1 patients without neoadjuvant therapy; Ex: 51 T2 patients without neoadjuvant treatment |
| | Grimard, L. and H. Stern (2012). "Local excision and brachytherapy for sphincter preservation in rectal cancer: Results on a cohort of 70 patients." <u>Radiotherapy and Oncology</u> 103 : S163. | Ex | Patients with local recurrence were excluded from analyses |
| | Grimard, L., H. Stern, et al. (2009). "Brachytherapy and local excision for sphincter preservation in T1 and T2 rectal cancer." Int J Radiat Oncol Biol Phys 74 (3): 803-809. | In | 51 T1, 84 T2, and 61 T3 patients. T2 and T3 patients were treated with preoperative radiotherapy |
| | Guerrieri, M., M. Baldarelli, et al. (2008). "Transanal endoscopic microsurgery for the treatment of selected patients with distal rectal cancer: 15 years experience." <u>Surg</u> <u>Endosc</u> 22 (9): 2030-2035. | | On request (included by Hingorani's and Smith's review) |
| | Habr-Gama, A., J. Gama-Rodrigues, et al. (2008). "Late assessment of local control by PET in patients with distal rectal cancer managed non-operatively after complete tumor regression following neoadjuvant chemoradiation." <u>Tech</u> <u>Coloproctol</u> 12 (1): 74-76. | | On request |
| | Han, S. L., Q. Q. Zeng, et al. (2010). "The indication and surgical results of local excision following radiotherapy for low rectal cancer." <u>Colorectal Dis</u> 12 (11): 1094-1098. | Ex | Results not presented separately per stage and per procedure |
| | Hazard, L. J., D. C. Shrieve, et al. (2009). "Local Excision vs. Radical Resection in T1-2 Rectal Carcinoma: Results of a Study From the Surveillance, Epidemiology, and End Results (SEER) Registry Data." <u>Gastrointest Cancer Res</u> 3 (3): 105-114. | Ex | 3.1% of 283 patients treated with local excision and radiotherapy had received radiotherapy preoperatively |
| 80 | Hompes, R., N. Mortensen, et al. (2012). "Exploring the role of minimally invasive treatment strategies in early rectal cancer: The significance of functional outcome and quality of life." <u>Surgical Endoscopy and Other Interventional Techniques</u> 26 (2): 582-583. | Ex | Short follow-up |
| | Hompes, R., F. Ris, et al. (2012). "Transanal glove port is a safe and cost-effective alternative for transanal endoscopic microsurgery." <u>Br J Surg</u> 99 (10): 1429-1435. | Ex | Short follow-up |
| | Hotta, K., T. Fujii, et al. (2009). "Local recurrence after | Ex | Endoscopic resection |

| | Reference | In- /Excluded | Reason(s) |
|-----|--|------------------|--|
| | endoscopic resection of colorectal tumors." <u>Int J Colorectal</u> <u>Dis</u> 24 (2): 225-230. | | |
| | Huh, J. W., E. J. Jung, et al. (2008). "Preoperative chemoradiation followed by transanal excision for rectal cancer." J Surg Res 148 (2): 244-250. | In | 9 patients with neoadjuvant treatment (1 T2, 8 T3) |
| | Huh, J. W., Y. A. Park, et al. (2009). "Recurrences after local excision for early rectal adenocarcinoma." <u>Yonsei Med J</u> 50 (5): 704-708. | Ex | Patients with neoadjuvant chemoradiation were excluded |
| | Ibarzabal, A., S. Delgado, et al. (2011). "MA-NOS colorectal resections: Our experience in malignant disease." <u>Surgical Endoscopy and Other Interventional Techniques</u> 25 : S29. | Ex | Not a local treatment |
| | Ikematsu, H., Y. Yoda, et al. (2012). "A large scale multi-center study of long-term outcomes after resection for submucosal invasive colorectal cancer (colon vs. rectum)." <u>Gastrointestinal Endoscopy</u> 1): AB178. | Ex | On endoscopic resection |
| | Inoue, Y., K. Togashi, et al. (2009). "Risk factors for relapse of T1 stage colorectal cancer resected endoscopically." <u>Gastroenterology</u> 1): A751. | Ex | On endoscopic resection |
| | Issa, N., I. Igov, et al. (2011). "Transanal endoscopic microsurgery for upper rectal tumors." <u>Colorectal Disease</u> 13 : 25. | | On request |
| | Issa, N., Y. Melki, et al. (2010). "Transanal endoscopic microsurgery for rectal tumor." <u>Techniques in Coloproctology</u> 14 (1) : 90. | Ex | Not reported how many patients with T1 were included; for T2 and T3 patients it was unclear whether neoadjuvant therapy was given |
| 90 | Issa, N., A. Murninkas, et al. (2012). "Long-term outcome of local excision after complete pathological response to neoadjuvant chemoradiation therapy for rectal cancer." <u>World J Surg</u> 36 (10): 2481-2487. | Ex | Biased sample of patients treated by local excision after neoadjuvant chemoradiotherapy: only the 23 patients whom were exclusively treated by local excision were followed up, and not the 8 patients whom had residual tumor after local excision and underwent radical excision subsequently |
| | Issa, N., A. Murninkas, et al. (2010). "Long-term results of local excision for rectal cancer for those with complete rectal wall response following neoadjuvant therapy." <u>Colorectal Disease</u> 12 : 14. | | On request |
| | Iversen, L. H. (2012). "Aspects of survival from colorectal cancer in Denmark." <u>Danish Medical Journal</u> 59 (4). | | On request |
| | Jamal, W. and S. Benoist (2010). "Transanal endoscopic microsurgery." <u>J Visc Surg</u> 147 (3): e161-165. | | On request |
| | Jeong, W. K., J. W. Park, et al. (2009). "Transanal endoscopic microsurgery for rectal tumors: experience at Korea's National Cancer Center." <u>Surg Endosc</u> 23 (11): 2575-2579. | Ex | Unclear how many patients were clinical T1 or T2. T2 patients did not get neoadjuvant therapy.; 3 T3 patients received neoadjuvant therapy |
| 95 | Jimenez, F., M. Conde, et al. (2012). "Local excision of rectal cancer in selected patients with T1 and T2 tumours: 25-year results." <u>Colorectal Disease</u> 14 : 50. | | On request |
| | Jin, Z., L. Yin, et al. (2010). "Anorectal functional results after transanal endoscopic microsurgery in benign and early malignant tumors." <u>World J Surg</u> 34 (5): 1128-1132. | Ex | Other outcomes (QoL at 6 months); not reported separately for the 13 patients with carcinoma |
| | Jung, W. H., A. P. Yoon, et al. (2009). "Recurrences after local excision for early rectal adenocarcinoma." <u>Yonsei Medical</u> <u>Journal</u> 50 (5): 704-708. | Ex | Patients with preoperative chemoradiation were excluded |
| | Kennelly, R. P., A. Heeney, et al. (2012). "A prospective analysis of patient outcome following treatment of T3 rectal cancer with neo-adjuvant chemoradiotherapy and transanal excision." <u>Int J Colorectal Dis</u> 27 (6): 759-764. | In | 10 T3 patients treated with local excision after neoadjuvant chemoradiotherapy |
| | Kesisoglou, I. and K. Sapalidis (2010). "Treatment of early rectal cancer." <u>Tech Coloproctol</u> 14 Suppl 1 : S33-34. | | On request |
| 100 | Kim, E., J. M. Hwang, et al. (2008). "Local excision for rectal | | On request |

| | Reference | ln- /Excluded | Reason(s) |
|-----|---|------------------|---|
| | carcinoma." <u>Clin Colorectal Cancer</u> 7(6): 376-385. | | |
| | Kiriyama, S., Y. Saito, et al. (2011). "Comparing endoscopic | Ex | All non-invasive tumors |
| | submucosal dissection with transanal resection for non- | | |
| | invasive rectal tumor: a retrospective study." J Gastroenterol | | |
| | <u>Hepatol</u> 26 (6): 1028-1033. | | |
| | Koebrugge, B., K. Bosscha, et al. (2009). "Transanal | Ex | Outcomes not specified by stage; T2 |
| | endoscopic microsurgery for local excision of rectal lesions: is | | patients did not receive neoadjuvant |
| | there a learning curve?" <u>Dig Surg</u> 26 (5): 372-377. | | therapy |
| | Kogler, P., R. Kafka-Ritsch, et al. (2012). "Is limited surgery | Ex | 29 T1 patients, neoadjuvant therapy not |
| | justified in the treatment of T1 colorectal cancer?" Surg | | mentioned |
| | Endosc. | | |
| | Kondylis, P. D. (2009). "Transanal endoscopic microsurgery | Ex | Abstract of another primary article |
| | for the treatment of rectal cancer: Comparison of wound | | |
| | complication rates with and without neoadjuvant radiation | | |
| | therapy." Diseases of the Colon and Rectum 52(12): 2057. | | |
| | Kopelman, Y., P. D. Siersema, et al. (2012). "Endoscopic full- | Ex | Narrative review |
| | thickness GI wall resection: current status." <u>Gastrointest</u> | | |
| | <u>Endosc</u> 75 (1): 165-173. | | |
| | Kreissler-Haag, D., J. Schuld, et al. (2008). "Complications | Ex | Short follow-up |
| | after transanal endoscopic microsurgical resection correlate | | |
| | with location of rectal neoplasms." <u>Surg Endosc</u> 22(3): 612- | | |
| | 616. | | |
| | Kundel, Y., R. Brenner, et al. (2008). "Is local excision after | Ex | Abstract of a study that is included for full |
| | complete pathological response to neoadjuvant | LA | text evaluation (Kundel 2010) |
| | chemoradiation for rectal cancer an acceptable treatment | | |
| | option?" <u>Annals of Oncology</u> 19 (58) : viii143. | | |
| | | In | 14 T1-T4 patients treated with neoadjuvant |
| | Kundel, Y., R. Brenner, et al. (2010). "Is local excision after | | therapy |
| | complete pathological response to neoadjuvant | | licity |
| | chemoradiation for rectal cancer an acceptable treatment | | |
| | option?" <u>Dis Colon Rectum</u> 53 (12): 1624-1631. | | |
| | Lebedyev, A., H. Tulchinsky, et al. (2009). "Long-term results | | On request |
| | of local excision for T1 rectal carcinoma: the experience of | | |
| 110 | two colorectal units." <u>Tech Coloproctol</u> 13 (3): 231-236. | - | |
| 110 | Lee, S. H., S. W. Jeon, et al. (2009). "A comparison of | Ex | Neoadjuvant therapy not mentioned |
| | transanal excision and endoscopic resection for early rectal | | |
| | cancer." <u>World J Gastrointest Endosc</u> 1(1): 56-60. | _ | |
| | Leonard, D., J. F. Colin, et al. (2012). "Transanal endoscopic | Ex | In: 5 T1 patients, neoadjuvant therapy not |
| | microsurgery: long-term experience, indication expansion, | | mentioned. Ex: 4 T2/T3 patients, neoadjuvant therapy not mentioned |
| | and technical improvements." <u>Surg Endosc</u> 26 (2): 312-322. | | |
| | Levic, K., O. Bulut, et al. (2011). "Early salvage surgery after | | On request |
| | TEM for rectal cancer: Is it oncologically safe?" Colorectal | | |
| | <u>Disease</u> 13 : 37. | | |
| | Lezoche, E., M. Baldarelli, et al. (2012). "Randomized clinical | In | RCT of TEM vs TME in T2 patients after |
| | trial of endoluminal locoregional resection versus | | neoadjuvant therapy |
| | laparoscopic total mesorectal excision for T2 rectal cancer | | |
| | after neoadjuvant therapy." <u>British Journal of Surgery</u> 99(9): | | |
| | 1211-1218. | | |
| | Lezoche, G., M. Baldarelli, et al. (2008). "A prospective | In | RCT of TEM vs TME in T2 patients after |
| | randomized study with a 5-year minimum follow-up | | neoadjuvant therapy |
| | evaluation of transanal endoscopic microsurgery versus | | |
| | laparoscopic total mesorectal excision after neoadjuvant | | |
| | therapy." <u>Surg Endosc</u> 22 (2): 352-358. | | |
| | Lezoche, G., M. Guerrieri, et al. (2011). "Transanal endoscopic | Ex | 135 T1-T2 patients; T2 patients received |
| | microsurgery for 135 patients with small nonadvanced low | | neoadjuvant therapy |
| | rectal cancer (iT1-iT2, iN0): short- and long-term results." | | |
| | <u>Surg Endosc</u> 25 (4): 1222-1229. | | |
| | Lezoche, G., A. M. Paganini, et al. (2012). "The role of | | On request |
| | locoregional resection with TEM to treat small nonadvanced | | |
| | low rectal cancer: The key point to obtaining good results." | | |
| | | | |

| | Reference | ln- /Excluded | Reason(s) |
|-----|---|------------------|--|
| | 26 (2): 584-585. | | |
| | Liang, H. H., C. C. Tu, et al. (2012). ""Air Bubble" in the Head after Transanal Excision of a Rectal Carcinoma." <u>J Emerg Med</u> . | Ex | Single case |
| | Lim, S. B., S. I. Seo, et al. (2012). "Feasibility of transanal minimally invasive surgery for mid-rectal lesions." <u>Surg Endosc</u> 26 (11): 3127-3132. | | On request |
| | Loder, P. (2012). "Endoscopic resection of colorectal cancer for cure: are we there yet?" <u>J Gastroenterol Hepatol</u> 27 (6): 995-996. | Ex | Editorial |
| 120 | Lorenz, C., T. Nimmesgern, et al. (2010). "Transanal single port microsurgery (TSPM) as a modified technique of transanal endoscopic microsurgery (TEM)." <u>Surg Innov</u> 17 (2): 160-163. | Ex | Short follow-up |
| | Lu, C. C., S. E. Lin, et al. (2012). "Comparison of clinical outcome of single-incision laparoscopic surgery using a simplified access system with conventional laparoscopic surgery for malignant colorectal disease." <u>Colorectal Disease</u> 14 (4): e171-e176. | Ex | Not a local excision procedure |
| | Luglio, G., V. Celentano, et al. (2011). "Functional and oncological outcomes after transanal local excision for rectal cancer. A prospective study." <u>European Journal of Surgical</u> <u>Oncology</u> 37 (12) : S4 | In | 16 T1 patients, offered preoperative radiotherapy |
| | Maas, M., D. Lambregts, et al. (2010). "Local excision for T1- 2N0 rectal cancer: Safe selection with lymph node specific contrast-enhanced MRI." <u>Colorectal Disease</u> 12 : 4. | | On request |
| | Maas, M., D. M. J. Lambregts, et al. (2010). "Selection of rectal cancer patients eligible for local excision with lymph node specific contrast-enhanced MRI." <u>European Journal of Surgical Oncology</u> 36 (9) : 817-818. | | On request |
| | Marakis, G., H. Demetriades, et al. (2009). "Local excision for rectal cancersafety and efficacy challenges." <u>Ann Surg Oncol</u> 16 (8): 2369-2370; author reply 2371-2362. | Ex | Letter, no observational data included |
| | Marks, J. H., J. L. Frenkel, et al. (2011). "Maximizing Rectal Cancer Results: TEM and TATA Techniques to Expand Sphincter Preservation." <u>Surgical Oncology Clinics of North</u> <u>America</u> 20 (3): 501-520. | | On request |
| | Marks, J. H., E. B. Valsdottir, et al. (2009). "Transanal endoscopic microsurgery for the treatment of rectal cancer: comparison of wound complication rates with and without neoadjuvant radiation therapy." <u>Surg Endosc</u> 23 (5): 1081-1087. | Ex | Short follow-up |
| | Meining, A., S. von Delius, et al. (2011). "Risk factors for unfavorable outcomes after endoscopic removal of submucosal invasive colorectal tumors." <u>Clin Gastroenterol</u> <u>Hepatol</u> 9 (7): 590-594. | Ex | Endoscopic resection |
| | Meyer, J. E. and D. L. Sherr (2009). "When less is more, when less is less: local excision in early rectal cancer." <u>Gastrointest</u> <u>Cancer Res</u> 3 (3): 123-124. | Ex | Editorial |
| 130 | Mittal, R., B. Perakath, et al. (2010). "Transanal excision of anorectal lesionsa single centre experience." <u>Trop</u> <u>Gastroenterol</u> 31 (1): 65-68. | | On request |
| | Mizrahi, B., J. Marks, et al. (2009). "T2 rectal cancer: A comparison of radical surgery and local excision by transanal endoscopic microsurgery (TEM) following neoadjuvant therapy." <u>Diseases of the Colon and Rectum</u> 52 (4) : 815-816. | | On request |
| | Mlkvy, P., J. Majek, et al. (2010). "Endoscopic treatment of praecancerous colorectal lesions and early colorectal cancer." <u>Bratisl Lek Listy</u> 111 (1): 50-53. | Ex | Narrative review |
| | Moore, J. S., P. A. Cataldo, et al. (2008). "Transanal | Ex | Not mentioned whether T2-3 patient hah had neoadjuvant therapy. Outcomes not |

| | Reference | ln- /Excluded | Reason(s) |
|-----|---|------------------|---|
| | endoscopic microsurgery is more effective than traditional transanal excision for resection of rectal masses." <u>Dis Colon</u> <u>Rectum</u> 51 (7): 1026-1030; discussion 1030-1021. | | reported per stage |
| | Morino, M., M. E. Allaix, et al. (2011). "Risk factors for recurrence after transanal endoscopic microsurgery for rectal malignant neoplasm." <u>Surg Endosc</u> 25 (11): 3683-3690. | Ex | 48 T1 patients, no neoadjuvant therapy; 5 T2 patients with neoadjuvant radiotherapy. 38 T2 patients and 16 P3 patients without neoadjuvant therapy |
| | Morino, M., A. Arezzo, et al. (2010). "Transanal endoscopic microsurgery for rectal neoplasms. An experience of 333 consecutive cases." <u>Techniques in Coloproctology</u> 14 (1) : 79. | Ex | Unclear how many patients had T1 |
| | Morino, M., A. Arezzo, et al. (2010). "Transanal endoscopic microsurgery for malignant rectal neoplasm. Results of 104 consecutive patients." <u>Techniques in Coloproctology</u> 14 (1) : 79. | Ex | 46 T1 patients, neoadjuvant therapy not mentioned;. preoperative radiotherapy given in an unknown number of T2 patients |
| | Nair, R. M., E. M. Siegel, et al. (2008). "Long-term results of transanal excision after neoadjuvant chemoradiation for T2 and T3 adenocarcinomas of the rectum." J Gastrointest Surg 12 (10): 1797-1805; discussion 1805-1796. | In | 22 T3 patients and 11 T2-3N1 patientstreated with local excision after neoadjuvant chemoradiation |
| | Nash, G. M., M. R. Weiser, et al. (2009). "Long-term survival after transanal excision of T1 rectal cancer." <u>Dis Colon</u> <u>Rectum</u> 52 (4): 577-582. | | On request |
| | Ngamruengphong, S., M. D. Crowell, et al. (2010). "Long term cancer-free survival is similar with either endoscopic or surgical treatment of malignant colo-rectal polyps - Report of an analysis of the Surveillance, Epidemiology, and End Results database." <u>Gastrointestinal Endoscopy</u> 71 (5) : AB129. | Ex | Endoscopic treatment |
| 140 | Nieuwenhuis, D. H., W. A. Draaisma, et al. (2009). "Transanal endoscopic operation for rectal lesions using two- dimensional visualization and standard endoscopic instruments: a prospective cohort study and comparison with the literature." <u>Surg Endosc</u> 23 (1): 80-86. | Ex | Short follow-up |
| | Oka, S., S. Tanaka, et al. (2011). "Mid-term prognosis after endoscopic resection for submucosal colorectal carcinoma: summary of a multicenter questionnaire survey conducted by the colorectal endoscopic resection standardization implementation working group in Japanese Society for Cancer of the Colon and Rectum." Dig Endosc 23 (2): 190-194. | Ex | Endoscopic resection |
| | Palma, P., K. Horisberger, et al. (2009). "Local excision of early rectal cancer: is transanal endoscopic microsurgery an alternative to radical surgery?" <u>Rev Esp Enferm Dig</u> 101 (3): 172-178. | Ex | 34 T1 patients, neoadjuvant therapy not mentioned |
| | Park, S. U., Y. W. Min, et al. (2011). "Comparison of clinical outcomes between the endoscopic submucosal dissection and the transanal endoscopic microsurgery for early rectal cancers." <u>Gastrointestinal Endoscopy</u> 1): AB305. | Ex | Stage of patients not mentioned; neoadjuvant therapy not mentioned; time of follow-up not mentioned |
| | Peng, J., W. Chen, et al. (2011). "Oncological outcome of T1 rectal cancer undergoing standard resection and local excision." <u>Colorectal Dis</u> 13 (2): e14-19. | Ex | 58 T1 patients, neoadjuvant therapy not mentioned |
| | Peng, J., W. Chen, et al. (2011). "Long-term outcome of early- stage rectal cancer undergoing standard resection and local excision." <u>Clin Colorectal Cancer</u> 10 (1): 37-41. | Ex | Patients who received postoperative therapy were excluded from analysis. Neoadjuvant therapy not mentioned |
| | Peng, J., Y. Xu, et al. (2010). "Outcome of T1N0 rectal cancer undergoing standard resection and local excision." <u>Diseases</u> of the Colon and Rectum 53 (4) : 638. | Ex | Neoadjuvant treatment not mentioned |
| | Penninckx, F. (2008). "Organ preservation in rectal cancer." <u>British Journal of Surgery</u> 95 (3): 269-270. | | On request |
| | Perez, R. O., A. Habr-Gama, et al. (2011). "Transanal endoscopic microsurgery for residual rectal cancer after neoadjuvant chemoradiation therapy is associated with significant immediate pain and hospital readmission rates." <u>Dis Colon Rectum</u> 54 (5): 545-551. | Ex | Other outcome (complications) |

| Reference | In- /Excluded | Reason(s) |
|--|------------------|--|
| Perez, R. O., A. Habr-Gama, et al. (2013). "Tran Endoscopic Microsurgery for Residual Rectal Cancer (yp Following Neoadjuvant Chemoradiation Therapy: An Word of Caution." <u>Dis Colon Rectum</u> 56 (1): 6-13. | T0-2) | 27 T2 patients treated with neoadjuvant therapy |
| 150 Pierce, R. and M. Whiteford (2010). "A comparison minimally invasive treatments for rectal tumors: TEN laparoscopic TME." <u>Diseases of the Colon and Rectum</u> 5 704-705. | v1 vs. | On request |
| Platell, C. (2009). "Transanal endoscopic microsurgery." Surg 79 (4): 275-280. | ANZ J Ex | Outcomes not reported per stage |
| Ragupathi, M. and E. M. Haas (2011). "Transanal endos video-assisted excision: application of single-port acc JSLS 15(1): 53-58. | | Narrative review |
| Ragupathi, M., D. V. Maele, et al. (2012). "Tran endoscopic video-assisted (TEVA) excision." <u>Surg Er</u> 26 (12): 3528-3535. | | Short follow-up |
| Ramani, V. S., A. Sun Myint, et al. (2011). "Local excision contact radiotherapy (CXR) for early rectal cancer: A s institution experience." <u>Radiotherapy and Oncology</u> 99 : 5 | single | Neoadjuvant therapy not mentioned |
| Ramirez, J. M., V. Aguilella, et al. (2011). "Tran endoscopic microsurgery for rectal cancer. Long oncologic results." <u>Int J Colorectal Dis</u> 26 (4): 437-443. | -term | No neoadjuvant treatment |
| Rizzuto, A., F. U. Zittel, et al. (2012). "Transanal Single Surgery (TAMIS) for the resection of small non advanced rectal cancer (iT1-iT2, IN0)." <u>European Journal of Su</u> <u>Oncology</u> 38 (9) : 791-792. | d low | On request |
| Rocha, J. J. and O. Feres (2008). "Transanal endos operation: a new proposal." <u>Acta Cir Bras</u> 23 Suppl 1 : 93 discussion 104. | | Neoadjuvant therapy not mentioned |
| Rothenberger, D. A. and D. Christoforidis (2008). " excision of distal rectal cancer: An update of cancer leukemia group B 8984 - Commentary." <u>Diseases of the c</u> <u>and Rectum</u> 51 (8): 1191-1193. | r and | On request |
| Ruiz-Tovar, J., J. Jimenez-Miramon, et al. (2010). "Endos resection as unique treatment for early colorectal car <u>Rev Esp Enferm Dig</u> 102 (7): 435-441. | | Narrative review |
| 160 Saito, N., Y. Nishizawa, et al. (2011). "Local therapy for risk T1 rectal cancer." <u>Colorectal Disease</u> 13: 20. | high- | On request |
| Salama, M., D. Ormonde, et al. (2010). "Outcome endoscopic resection of large colorectal neoplasms Australian experience." <u>J Gastroenterol Hepatol</u> 25 (1): 84 | s: an | Endoscopic resection |
| Seman, M., F. Bretagnol, et al. (2010). "Transanal endos microsurgery (TEM) for rectal tumor: the first French s center experience." <u>Gastroenterol Clin Biol</u> 34 (8-9): 488- | ingle- | On request |
| Serra-Aracil, X., H. Vallverdu, et al. (2008). "Long-term for up of local rectal cancer surgery by transanal endos microsurgery." <u>World J Surg</u> 32 (6): 1162-1167. | | No neoadjuvant therapy |
| Sgourakis, G., S. Lanitis, et al. (2011). "Transanal endos microsurgery for T1 and T2 rectal cancers: a meta-an and meta-regression analysis of outcomes." <u>Am Surg</u> 7 761-772. | alysis | Used for reference tracking |
| Shelygin, Y., I. Peresada, et al. (2011). "Organ-s treatment for early rectal carcinomas." <u>Colorectal Diseas</u> 42. | <u>se</u> 13: | Series of 23 T1-3 patients treated by TEM, unclear how many received neoadjuvant therapy as this is not described systematically. At least 1 patient did, as: 'The distant recurrence was in a patient with significant medical comorbidities who underwent neoadjuvant chemoradiation and TEM for a clinical T2 tumor' |
| Slack, T., S. Wong, et al. (2012). "Transanal minimally inv surgery: an initial experience." <u>ANZ J Surg</u> . | asive | On request |

| Reference | ln- /Excluded | Reason(s) |
|---|------------------|---|
| Speake, D., N. Lees, et al. (2008). "Who should be followed up after transanal endoscopic resection of rectal tumours?" <u>Colorectal Dis</u> 10 (4): 330-335. | Ex | Patients who had immediate salvage surgery were not followed |
| Steinhagen, E., G. Chang, et al. (2011). "Initial experience with transanal endoscopic microsurgery: the need for understanding the limitations." <u>J Gastrointest Surg</u> 15 (6): 958-962. | | On request |
| Stipa, F., V. Giaccaglia, et al. (2012). "Management and outcome of local recurrence following transanal endoscopic microsurgery for rectal cancer." <u>Dis Colon Rectum</u> 55 (3): 262-269. | Ex | 86 T1 patients without neoadjuvant chemotherapy.T2-3 patients: 'preoperative chemoradiation was administered to 37 patients (25.7%) with T2 or T3 tumors' |
| 170 Stylinski, R., T. Pedowski, et al. (2011). "TEM (Transanal Endoscopic Microsurgery) in rectal cancer - Own experience." <u>European Surgery - Acta Chirurgica Austriaca</u> 43: 12-13. | | On request |
| Suppiah, A., S. Maslekar, et al. (2008). "Transanal endoscopic microsurgery in early rectal cancer: time for a trial?" Colorectal Dis 10 (4): 314-327; discussion 327-319. | Ex | No quality appraisal (used for reference tracking) |
| Tarantino, I., F. H. Hetzer, et al. (2008). "Local excision and endoscopic posterior mesorectal resection versus low anterior resection in T1 rectal cancer." <u>Br J Surg</u> 95 (3): 375- 380. | | On request |
| Tarantino, I. and A. Zerz (2008). "Authors reply: Local excision and endoscopic posterior mesorectal resection versus low anterior resection in T1 rectal cancer (Br J Surg 2008; 95: 375- 380)." <u>British Journal of Surgery</u> 95 (7): 931. | | On request |
| Tennyson, N., W. M. Mendenhall, et al. (2011). "Transanal excision combined with either preoperative or postoperative radiation therapy for rectal adenocarcinoma: The university of Florida experience." <u>International Journal of Radiation</u> <u>Oncology Biology Physics</u> 1): S373. | Ex | Abstract of Tennyson 2012 |
| Tennyson, N., W. M. Mendenhall, et al. (2012). "Transanal excision with radiation therapy for rectal adenocarcinoma." <u>Clin Med Res</u> 10 (4): 224-229. | ? | 26/38 T1-3 patients were treated with preoperative radiotherapy |
| Toyonaga, T., M. Man-i, et al. (2010). "Endoscopic treatment for early stage colorectal tumors: the comparison between EMR with small incision, simplified ESD, and ESD using the standard flush knife and the ball tipped flush knife." <u>Acta Chir</u> <u>lugosl</u> 57 (3): 41-46. | | On request |
| Trostchansky, I., A. Shalabi, et al. (2011). "Excision of rectal tumors using transanal endoscopic microsurgery." <u>Techniques in Coloproctology</u> 15 (1) : 116. | Ex | Neoadjuvant therapy not mentioned |
| Tsai, B., C. Finne, et al. (2009). "Transanal endoscopic microsurgery (TEM) resection of rectal tumors: Outcomes and recommendations." <u>Diseases of the Colon and Rectum</u> 52 (4): 775. | Ex | Neoadjuvant therapy not mentioned |
| Tsai, B. M., C. O. Finne, et al. (2010). "Transanal endoscopic microsurgery resection of rectal tumors: outcomes and recommendations." Dis Colon Rectum 53 (1): 16-23. | | On request |
| 180 Tsai, B. M., C. O. Finne, et al. (2010). "Transanal endoscopic microsurgery resection of rectal tumors: Outcomes and recommendations." <u>Diseases of the Colon and Rectum</u> 53(1): 16-23. | | On request |
| Tytherleigh, M. G., B. F. Warren, et al. (2008). "Management of early rectal cancer." <u>The British journal of surgery</u> 95 (4): 409-423. | Ex | Narrative review, no original observational data |
| van den Broek, F. J., E. J. de Graaf, et al. (2009). "Transanal endoscopic microsurgery versus endoscopic mucosal resection for large rectal adenomas (TREND-study)." <u>BMC</u> <u>Surg</u> 9 : 4. | Ex | On adenomas |
| Van Leerdam, M. E., T. C. Smyrk, et al. (2010). "Long term | Ex | Neoadjuvant therapy not mentioned |

| | Reference | In- /Excluded | Reason(s) |
|-----|---|------------------|---|
| | outcome of early colorectal cancer treated with local excision or radical resection." <u>Gastroenterology</u> 1): S44 | | |
| | Walega, P., J. Kenig, et al. (2009). "Combination of TEM and | | On request |
| | EPMR in the treatment of patients with T1 rectal cancer." <u>Colorectal Disease</u> 11 : 56. | | |
| | Walega, P., J. Kenig, et al. (2010). "Functional and clinical results of transanal endoscopic microsurgery combined with endoscopic posterior mesorectum resection for the treatment of patients with t1 rectal cancer." <u>World J Surg</u> | Ex | 6 T1 patients treated by TEM. Neoadjuvant therapy not mentioned |
| | 34 (7): 1604-1608. Walega, P., J. Kenig, et al. (2010). "Transanal endoscopic microsurgery (TEM) combined with endoscopic posterior mesorectum excision in the treatment of patients with T1 rectal cancer: Own results." <u>Colorectal Disease</u> 12 : 14. | Ex | 8 T1 patients treated by TEM. Neoadjuvant therapy not mentioned |
| | Walega, P., J. Kenig, et al. (2010). "Transanal endoscopic microsurgery combined with endoscopic posterior mesorectum excision in the treatment of patients with T1 rectal cancer: Own results." <u>Annals of Oncology</u> 21 : vi108-vi109. | | On request |
| | Walega, P., J. Kenig, et al. (2012). "Functional and clinical results of T1 rectal cancer treatment using transanal endoscopic microsurgery combined with endoscopic posterior mesorectum resection." <u>Colorectal Disease</u> 14 : 61. | | On request |
| | Whitehouse, P. A., J. N. Armitage, et al. (2008). "Transanal endoscopic microsurgery: local recurrence rate following resection of rectal cancer." <u>Colorectal Dis</u> 10 (2): 187-193. | | On request |
| 190 | Wildbore, P. (2008). "Population-based study of local surgery for rectal cancer (Br J Surg 2007; 94: 1421-1426)." <u>Br J Surg</u> 95 (2): 262; author reply 262. | Ex | Letter with no additional information |
| | Wortham, A. H., D. Schreiber, et al. (2009). "Overall survival using local excision techniques with and without radiation compared with APR for stage I rectal cancer: A SEER based analysis." Journal of Clinical Oncology 1): 4032. | | On request |
| | Wu, Y., Y. Y. Wu, et al. (2011). "TEM and conventional rectal surgery for T1 rectal cancer: A meta-analysis." <u>Hepato-Gastroenterology</u> 58 (106): 364-368. | | On request |
| | Wu, Z. Y., G. Zhao, et al. (2012). "Oncological outcomes of transanal local excision for high risk T(1) rectal cancers." <u>World J Gastrointest Oncol</u> 4 (4): 84-88. | Ex | T1 patients without neoadjuvant treatment |
| | Yeh, Y. S., M. J. Chen, et al. (2012). "Transanal inside-out rectal resection for ultra-low rectal cancer." <u>J Invest Surg</u> 25 (6): 375-380. | | On request |
| | Yeo, S. G., D. Y. Kim, et al. (2010). "Local excision following pre-operative chemoradiotherapy-induced downstaging for selected cT3 distal rectal cancer." Jpn J Clin Oncol 40 (8): 754-760. | In | 11 T3 patients, local excision after neoadjuvant chemoradiotherapy |
| | Yi, H., H. Yong-Gang, et al. (2012). "Local Resection for Rectal Tumors: Comparative Study of Transanal Endoscopic Microsurgery versus Conventional Transanal Excision - The Experience in China." <u>Hepatogastroenterology</u> 59 (120). | Ex | 17 T1 patients, neoadjuvant therapy not mentioned. 4 T2 patients, neoadjuvant therapy not mentioned |
| | Yin, L., Y. G. He, et al. (2011). "Local surgical treatment of rectal tumors." <u>Techniques in Coloproctology</u> 15 (1) : 122. | Ex | Neoadjuvant therapy not mentioned |
| | Yoda, Y., H. Ikematsu, et al. (2010). "Long-term outcomes after endoscopic resection for submucosal invasive colorectal cancer." <u>Gastrointestinal Endoscopy</u> 71 (5) : AB340. | Ex | On endoscopic resection |
| | Yoda, Y., H. Ikematsu, et al. (2011). "A large scale multi-center study of long-term outcomes after endoscopic resection for submucosal invasive colorectal cancer." <u>Gastrointestinal</u> | Ex | On endoscopic resection |
| | Endoscopy 1): AB296-AB297. | Ex | Patients with preoperative chemotherapy o |

| | Reference | ln- /Excluded | Reason(s) |
|-----|--|------------------|---|
| | transanal excision of T1 rectal cancer." <u>Journal of</u> <u>Gastroenterology and Hepatology</u> 26 : 132. | | radiotherapy were excluded |
| | You, Y. N. (2011). "Local excision: is it an adequate substitute for radical resection in T1/T2 patients?" <u>Semin Radiat Oncol</u> 21 (3): 178-184. | | On request |
| | Zhang, H., Y. S. Zhang, et al. (2012). "Transanal single-port laparoscopic total mesorectal excision in the treatment of rectal cancer." <u>Tech Coloproctol</u> . | | On request |
| | Zhao, D. B., Y. K. Wu, et al. (2009). "Prognostic factors for 5- year survival after local excision of rectal cancer." <u>World J</u> <u>Gastroenterol</u> 15 (10): 1242-1245. | Ex | 4/106 patients received preoperative radiotherapy |
| | Zhou, X., X. E. Huang, et al. (2011). "Extended full-thickness transanal local excision to treat ultra-low rectal cancer: an initial clinical exploration." <u>Asian Pac J Cancer Prev</u> 12 (4): 1045-1048. | Ex | Short follow-up |
| 205 | Ziogas, D., P. Tsekeris, et al. (2008). "Benefits, limitations, and harm of local excision for rectal cancer." <u>Ann Surg Oncol</u> 15 (9): 2628-2629; author reply 2630-2621 | Ex | Letter without original observational data |

Table 3. Studies identified through reference tracking and evaluated full text

| | Reference | In- | Reason(s) |
|----|--|-----------|-------------------------------------|
| 4 | | /Excluded | |
| 1 | Bonnen M, Crane C, Vauthey JN, et al. Long-term results using | In | 26 T3 patients after neoadjuvant |
| | local excision after preoperative hemoradiation among | | therapy |
| | selected T3 rectal cancer patients. Int J Radiat Oncol Biol Phys | | |
| | 2004; 60:1098–105 | | |
| | Borschitz, T., D. Wachtlin, et al. (2008). "Neoadjuvant chemoradiation and local excision for T2-3 rectal cancer." | In | 3 T3 patients after neoadjuvant |
| | | | therapy (table 2) |
| | Annals of surgical oncology 15(3): 712-720. | | |
| | Caricato M, Borzomati D, Ausania F, Tonini G, Rabitti C, Valeri | | On request |
| | S et al. Complementary use of local excision and transanal | | |
| | endoscopic microsurgery for rectal cancer after neoadjuvant | | |
| | chemoradiation. Surg Endosc 2006; 20: 1203–1207 | 10 | 11 T1 and 1 T2 actions with |
| | Hershman MJ, Myint AS, Makin CA. Multi-modality approach | In | 11 T1 and 4 T3 patients with |
| | in curative local treatment of early rectal carcinomas. Colorectal Dis 2003; 5:445–50 | | neoadjuvant therapy |
| 5 | | | On request |
| 5 | Kim CJ, Yeatman TJ, Coppola D, Trotti A, Williams B, Barthel | | On request |
| | JS, et al. Local excision of T2 and T3 rectal cancers after downstaging chemoradiation. Ann Surg 2001;234:352-358 | | |
| | Kim JC, Kim HC, Yu CS, et al. Efficacy of 3-dimensional | Ex | Outcomes not reported seperately |
| | endorectal ultrasonography compared with conventional | EX | for T2 vs. T3 patients |
| | ultrasonography and computed tomography in preoperative | | |
| | rectal cancer staging. Am J Surg 2006; 192:89–97 | | |
| | Lezoche E, Guerrieri M, Paganini AM, Feliciotti F. Long-term | | On request |
| | results of patients with pT2 rectal cancer treated with | | onrequest |
| | radiotherapy and transanal endoscopic microsurgical excision. | | |
| | World J Surg 2002; 26: 1170–1174. | | |
| | Lezoche E, Guerrieri M, Paganini AM, et al. Long-term results | In? | Outcomes not reported seperately |
| | in patients with T2–3 N0 distal rectal cancer undergoing | - | for clinical staging, but reported |
| | radiotherapy before transanal endoscopic microsurgery. Br J | | seperately for pathological staging |
| | Surg 2005; 92:1546–52 | | . , , |
| | Marks G, Mohiuddin MM, Masoni L, Pecchioli L. | | On request |
| | High-dose preoperative radiation and full-thickness local | | |
| | excision. A new option for patients with select cancers of the | | |
| | rectum. Dis Colon Rectum 1990; 33: 735–739. | | |
| 10 | Meadows K, Morris CG, Rout WR, Zlotecki RA, Hochwald SN, | | On request |
| | Marsh RD, et al. Preoperative radiotherapy alone or | | |

| | Reference | In- /Excluded | Reason(s) |
|----|--|------------------|--|
| | combined with chemotherapy followed by transanal excision for rectal adenocarcinoma. Am J Clin Oncol 2006;/29:/430_4 | | |
| | Mohiuddin M, Marks G, Bannon J. High-dose preoperative radiation and full thickness local excision: A new option for selected T3 distal rectal cancers. Int J Radiat Oncol Biol Phys 1994;30:845 – 9 | | On request |
| | Park C, LeeW, Han S, Yun S, Chun HK. Transanal local excision for preoperative concurrent chemoradiation therapy for distal rectal cancer in selected patients. Surg Today 2007; 37: 1068– 1072. | | On request |
| | Ruo L, Guillem JG, Minsky BD, et al. Preoperative radiation with or without chemotherapy and full-thickness transanal excision for selected T2 and T3 distal rectal cancers. Int J Colorectal Dis 2002; 17:54–8 | In | 4 T3 patients treated with neoadjuvant therapy |
| | Schell SR, Zlotecki RA, Mendenhall WM, et al. Transanal excision of locally advanced rectal cancers downstaged using neoadjuvant chemoradiotherapy. J Am Coll Surg 2002; 194:584–90 | In | 11 T3 patients treated neoadjuvantly |
| 15 | Stipa F, Lucandri G, Ferri M, Casula G, Ziparo V. Local excision of rectal cancer with transanal endoscopic microsurgery (TEM). Anticancer Res 2004;/24:/1167_72 | | On request |

SEARCH STRINGS

All searches were limited to studies published in English, from 2008 onwards.

4. MEDLINE, MEDLINE IN PROGRESS (VIA PUBMED)

"Colorectal neoplasms" [majr] OR ((colorectal OR rectal OR rectum OR rectosigmoid) AND (cancer* OR carcinoma* OR adenocarcinoma* OR malignan* OR tumor* OR tumour* OR neoplasm*))

AND

((local[ti] OR transanal*[ti] OR rectoscop* OR endoscop*[ti] OR limited[ti]) AND (surgery OR surgical* OR resect* OR excision OR treatment OR therapy) OR microsurgery[ti] OR microsurgical* OR spts OR parks)

AND (for systematic reviews)

("meta-analysis" [pt] OR "meta-anal*" [tw] OR "metaanal*" [tw] OR ("quantitativ* review*" [tw] OR "quantitative* overview*" [tw]) OR ("systematic* review*" [tw] OR "systematic* overview*" [tw]) OR ("methodologic* review*" [tw] OR "methodologic* overview*" [tw]) OR ("review" [pt] AND "medline" [tw])

5. EMBASE (VIA OVID)

For systematic reviews:

- 1 exp rectum cancer/dm, su, th [Disease Management, Surgery, Therapy] (20811)
- 2 (colorectal or rectum or rectal).tw. (193202)
- 3 (cancer* or carcinoma* or adenocarcinoma* or malignan* or tumor* or tumour* or neoplasm*).tw. (2536234)

4 2 and 3 (134197)

5 1 or 4 (137765)

- 6 exp Meta Analysis/ (67825)
- 7 ((meta adj analy\$) or metaanalys\$).tw. (63259)
- 8 (systematic adj (review\$1 or overview\$1)).tw. (48931)
- 9 or/6-8 (125331)
- 10 cancerlit.ab. (667)
- 11 cochrane.ab. (28826)
- 12 embase.ab. (25782)
- 13 (psychlit or psyclit).ab. (957)
- 14 (psychinfo or psycinfo).ab. (6385)
- 15 (cinahl or cinhal).ab. (8749)
- 16 science citation index.ab. (1914)
- 17 bids.ab. (425)
- 18 or/10-17 (44008)
- 19 reference lists.ab. (8636)
- 20 bibliograph\$.ab. (13882)
- 21 hand-search\$.ab. (3979)
- 22 manual search\$.ab. (2282)
- 23 relevant journals.ab. (724)
- 24 or/19-23 (26625)
- 25 data extraction.ab. (10625)
- 26 selection criteria.ab. (19440)
- 27 25 or 26 (28708)
- 28 review.pt. (1919543)
- 29 27 and 28 (17086)
- 30 letter.pt. (807623)
- 31 editorial.pt. (421593)
- 32 animal/ (1810429)
- 33 human/ (13958281)
- 34 32 not (32 and 33) (1354958)
- 35 or/30-31,34 (2570545)
- 36 9 or 18 or 24 or 29 (156522)

- 37 36 not 35 (150695)
- 38 microsurgery.mp. or exp microsurgery/ (29837)
- 39 microsurgical*.mp. (15065)
- 40 spts.mp. (680)
- 41 parks.mp. (2680)
- 42 exp local therapy/ (1657)
- 43 exp endoscopic submucosal dissection/ or exp endoscopic therapy/ or exp endoscopic surgery/ (137736)
- 44 or/38-43 (176199)
- 45 (local* or transanal* or endoscop* or limited or rectoscopic*).mp. (1884390)

46 (surgery or surgical* or resect* or excision or treatment or therapy).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword] (7009548)

- 47 45 and 46 (758460)
- 48 44 or 47 (868922)
- 49 5 and 37 and 48 (673)
- 50 limit 49 to (english language and yr="2008 -Current") (349)

For other studies:

- 1 microsurgery.ti. (4076)
- 2 exp microsurgery/ (26329)
- 3 microsurgical*.ti. (5274)
- 4 (spts or parks).ti. (590)

5 exp local therapy/ or exp endoscopic submucosal dissection/ or exp endoscopic therapy/ or exp endoscopic surgery/ (139361)

- 6 or/1-5 (166471)
- 7 (local* or transanal* or endoscop* or limited or rectoscopic*).ti. (283755)
- 8 (surgery or surgical* or resect* or excision or treatment or therapy).ti. (2004013)
- 9 7 and 8 (42007)
- 10 6 or 9 (197745)
- 11 exp rectum cancer/dm, su, th (20811)
- 12 (colorectal or rectum or rectal).ti. (103436)
- 13 (cancer* or carcinoma* or adenocarcinoma* or malignan* or tumor* or tumour* or neoplasm*).ti. (1560199)
- 14 12 and 13 (73425)

- 15 11 or 14 (80372)
- 16 10 and 15 (5593)
- 17 limit 16 to (english language and yr="2008 -Current") (2399)

6. CDSR (VIA THE COCHRANE LIBRARY)

The Cochrane Database of Systematic Reviews was browsed by topic:

a. cancer -> colorectal -> surgery

REFERENCES