**Kliiniline küsimus nr 1**

Kas patsiendi rasvtõve kirurgiline ravi vs konservatiivse ravimeetodiga on tulemuslikum?

**Tulemusnäitajad**:

1a. liigse kehakaalu ja KMI langus 2 - 5 ja enam aastat pärast bariaatrilist operatsiooni

1b. kaasuvate haiguste remissioon või taandumine

1c. kvaliteetselt elatud eluaastate lisandumine (QALY)

1d. patsiendi rahulolu raviga/ tulemusega,

1e. rasvumusega seotud haiguste esinemine, ravikulu vähenemine ( 5 aasta perspektiivis)

1f. töövõimetuse vähenemine.

**Kokkuvõte leitud kirjandusest**

Liigse kehakaalu languse pikaajalisi tulemusi rasvtõve kirurgilise ravi ja konservatiivse ravi gruppides hinnati 1 süstemaatilises ülevaates (Picot et al.2012), 1 randomiseeritud kontrolluuringus (RCT) (Mingrone 2012) ja 3 vaatlusuuringus (Sjöström 2012, Buddenberg 2006 ja Leslie 2011). Antud uuringud hõlmasid patsiente KMIga üle 30, koos või ilma kaasuvate haigusteta. Kaalulangust hinnati kas kehakaalu protsentuaalse muutusena, KMI muutusena või protsendina liigse kehakaalu langusest (%EWL). Uurimisperioodi pikkuseks erinevates uuringutes oli 2 – 15 aastat. Kõikides hõlmatud uuringutes esines suurem kehakaalu langus kirurgilise ravi gruppides (Tabel 1).

Samades uuringutes (v.a Buddenberg 2006) hinnati ka erinevate ravimeetodite mõju 2. tüüpi diabeedile (Tabel 1b). Ühes mitterandomiseeritud vaatlusuuringus(Sjöström 2012), mis ainsa uuringuna näitas 10 aasta andmeid, leiti, et võrreldes 2 aasta tulemustega oli 50%-l remissioonis diabeediga patsiendil haigus taastekkinud.Ülejäänud uuringutes tehti kokkuvõtted 2 aasta tulemustega. Kõikides hõlmatud uuringutes leiti statistiliselt oluline erinevus diabeedi remissioonis ja glükohemoblobiini väärtustes kirurgilise grupi kasuks.

2014 aastal ilmunud metaanalüüsis (Kwok et al.) võetakse kokku 14 prospektiivse ja retrospektiivse vaatlusuuringu andmed, mis hindavad erinevate rasvtõve ravimeetodite mõju kardiovaskulaarsetele haigustele ja suremusele. Kirurgilise ravi grupis oli 50% suremuse vähenemine võrreldes kontrollgrupiga (OR 0.48 95% CI 0.35-0.64, I2=86%). Statistiliselt oluliselt vähenes ka risk müokardi infarktile ja insuldile kirurglise ravi rühmas (vastavalt OR 0.46 95% CI 0.30-0.69, I2=79% ja OR 0.49 95% CI 0.32-0.75, I2=59%)

Üldnumbritena sündmute esinemissagedusest (absolute event rates) esines kirurgilise ravi grupis vähem kardiaalseid tüsistusi: surevus 3,6 vs 11,4%, müokardi infarkt 1,3 vs 2,5%, insult 0,8 vs 1,5%, muud kardiaalsed tüsistused 2,4 vs 4,0.

2015 aasta metaanalüüsis (Skubleny et al) näidati veenvalt bariaatriliste operatsioonide mõju polütsüstiliste munasarjade sündroomile ning sellega kaasnevatele kliinilistele ilmingutele – menstruaaltsükli häired, hirsutism, viljatus. 13 vaatlusuuringu analüüs näitas kaalulanguse positiivset mõju eelpoolnimetatud patoloogiatele.

Picot et al (2012) süstemaatilises ülevaates on hinnatud ka kvaliteetselt elatud eluaastate lisandumist (QALY) ning majanduslikku mõju rasvtõve ravis (Tabel 1c). Leiti, et ehkki kirurgiline ravi on lühiperspektiivis kallim, siis juba 2 aasta perspektiivis oli tõusnud QALY kirurgilise ravi grupis. Kasutades 20 aasta tõenäosus sensitiivsusanalüüsi olid kirurglise protseduuriga lisanduvad kulud negatiivsed. Täiendkulu tõhususe määr (ICER) 2 aastal oli 20159 naela, kuid 20 aastaks oli see ainult 1634 naela. Võtmeküsimuseks on T2DM-ga seotud tervishoiukulud.

2011 avaldatud süstemaatiline ülevaade (Padwal et al.) näitab 13 artikli majanduslikke tulemusi, kus on näidatud, et pikaajaline bariaatrilise kirurgia majanduslik kasulikkus tundub atraktiivne. ICUR (incremental cost utility ratio) ulatub 1000USD kuni 40000 USDni iga kvaliteetselt elatud eluaasta eest.

Soome 2011 a analüüsis (Mäklin et al.) on 10 aasta perspektiivis leitud, et operatiivne ravi (sleeve gastrectomy, RYGB) hakkab ennast ära tasuma juba 5 aasta pärast (6 aastat peale bandi). Elukvaliteedi muutused olid baasist kõrgemad ka 10 aastat peale sekkumist. Kui operatiivne ravi teostati BMIga alla 38 patsientidel oli 10 a perspektiivis kirurgiline ravi kallim, kuid efektiivsem.

Elukvaliteeti hinnati võrdlevalt 1 RCT ja 2 jälgimisuuringus.

O´Brien et al (2006)kasutasid oma uuringus SF-36 küsimustikku 2 aasta dünaamikas. 5 parameetris kaheksast oli statistiliselt oluline paranemine kirurgilist ravi saanute grupis.

Karlsson et al (2006) uuringus näidati, et baasväärtusena ei esinenud statistilist erinevust tervisetunnetuses, sotsialses suhtlemises, rasvumisega seotud probleemides, tujus ja depressioonis. 10 aasta tulemusena olid need tulemusnäitajad statistiliselt paremad kirurgilise ravi rühmas.

2013 a avaldatud vaatlusuuringus (Canetti et al.) leiti, et kasutades SF-36 küsimustikku, saavutasid kirurgilise ravi grupi patsiendi statistiliselt olulise paranemise kõikides 8- shinnatavas kriteeriumis. Konservatiivse ravi grupi patsientidel esines statistiliselt oluline paranemine 3/8 kriteeriumist.

Raviga rahulolu andmed on avaldanud oma uuringus Buddenberg et al. (2006). Leiti et operatsiooni järgselt ei esinenud statistilist olulist erinevust rahulolus kirurgilise ja mittekirurgilise ravi grupis.

Ehkki mitmetes artiklites on esile toodud kirurgilise ravi järgset füüisilse aktiivsuse ja seetõttu ka töövõime paranemist, on võrdlevad andmed avaldatud ainult Rootsi SOS uuringu raamides (Sjöström 2004). 6 aasta vältel peale sekkumist oli kirurgilise ravi grupis füüisliselt aktiivsete hulk suurem

**Kokkuvõte ravijuhenditest**

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| Ravijuhend | Ravijuhendis sisalduv tekst küsimuse kohta | Viited | Ravijuhendis hõlmatud kirjanduse otsingu ajavhemik |
| CLINICAL PRACTICE GUIDELINES FOR THE MANAGEMENT OF OVERWEIGHT AND OBESITY IN ADULTS, ADOLESCENTS AND CHILDREN IN **AUSTRALIA 2013** | Täiskasvanud ülekaalulistel on kaalulangetamiseks kirurgiline ravi efektiivsem võrreldes mittekirurgiliste kaalulangetamiste sekkumistega | **Buchwald H, Estok R, Fahrbach K et al. (2009**) Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. Am J Med 122(3): 248–56 e5.  **Colquitt JL, Picot J, Loveman E et al. (2009**) Surgery for obesity. Cochrane Database of Systematic Reviews DOI: 10.1002/14651858.CD003641.pub3.  **Dixon JB, O’Brien PE, Playfair J et al. (2008**) Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial. JAMA 299(3): 316–23.  **Maggard M, Shugarman L, Suttorp M et al. (2005)** Meta-analysis: surgical treatment of obesity. Ann Intern Med 142: 547–59.  **Mingrone G, Panunzi S, De Gaetano A et al. (2012)**Bariatric surgery versus conventional medical therapy for type 2 diabetes. N Engl J Med 366: 1577–85.  **O’Brien PE, Sawyer SM, Laurie C et al. (2010)** Laparoscopic adjustable gastric banding in severely obese adolescents: a randomized trial. JAMA 303(6): 519–26.  **Snow V, Barry P, Fitterman N et al. (2005)** Clinical Efficacy Assessment Subcommittee of the American College of Physicians. Pharmacologic and surgical management of obesity in primary care: a clinical practice guideline from the American College of Physicians. Ann Intern Med 142: 525–31. | Kuni juuli 2011 |
| Management of Obesity  SIGN 2010 | Võrreldes parima saadaoleva mitte-kirurgilise kaalulangetamise programmiga langeb bariaatrilise kirurgia järgselt oluliselt hypertriglütserideemia ja LHDL risk.  Bariaatrilise kirurgia läbinud patsientidest kes said kardiovaskulaarset ravi, vajasid 23% vähema tõenäosusega ravi 6 aastat hiljem.  Ühes uuringus leiti 10 aastat hiljem oluline paranemine tervise tajus, sotsiaalses suhtlemises ja depressiooni languses bariaatrilise kirurgi patsientidel.  5 uuringut esitavad andmed elukvaliteedi paranemises bariaatrilise kirurgia järgselt. | **Colquitt J, Clegg A, Loveman E, Royle P, Sidhu MK**. Surgery for  morbid obesity (Cochrane Review). In: The Cochrane Library, Issue  4, 2005. London: Wiley  **Karlsson J, Taft C, Ryden A, Sjostrom L, Sullivan M**. Ten-year trends  in health-related quality of life after surgical and conventional  treatment for severe obesity: The SOS intervention study. Int J  Obes 2007;31(8):1248-61.  **Mathus-Vliegen EMH, De Wit LT**. Health-related quality of life  after gastric banding. Br J Surg 2007;94(4):457-65.  **Champault A, Duwat O, Polliand C, Rizk N, Champault GG.**  Quality of life after laparoscopic gastric banding: Prospective study  (152 cases) with a follow-up of 2 years. Surg Laparosc Endosc  Percutan Tech 2006;16(3):131-6.  **Burgmer R, Petersen I, Burgmer M, de Zwaan M, Wolf AM,**  **Herpertz S**. Psychological outcome two years after restrictive  bariatric surgery. Obesity Surgery 2007;17(6):785-91.  **Buddeberg-Fischer B, Klaghofer R, Krug L, Buddeberg C, Muller**  **MK, Schoeb O, et al**. Physical and psychosocial outcome in  morbidly obese patients with and without bariatric surgery: a 4  1/2-year follow-up. Obesity Surgery 2006;16(3):321-30. | 2007 |
| National Institute for Healt and Clinical Excellence  NICE 2006 | Kirurgia seostus kliiniliste tulemuste (vererõhk, kolesterooli tase, triglütseriidide ja glükoosi tase) paranemisega võrreldes mittekirurgiliste patsientidega.  Kirurgia tulemused on ülekaalulistel patsientidel pikajalisetulemusena (10 aastat)efektiivsemad, kui mittekirgurgiilse sekkumisega | **Mingrone 2002 RCT**  **SOS Matched control cohort study** |  |

**Tabel 1a**

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| Autor/Aasta/  Uuringumeetod/  Tõendusmaterjali kvaliteedi (TK) hinnang | Uuringu kestvus | Patsientide arv | Ravimeetodid | Peamised tulemused |
| Mingrone et al. 2012  RCT  **TK - Kõrge** | 2 aastat | 60 | RYGB  BPD  Konservatiivne meetod | At 2 years, patients in the two surgical groups had greater percent reductions in average body weight from baseline than did patients receiving medical therapy (−4.74±6.37%), with−33.31±7.88% for gastric bypass and−33.82±10.17% forbiliopancreatic diversion (P<0.001 for both comparisons) |
| Sjöström et al.  2012  Mitte-randomiseeritud vaatlusuuring  **TK - Mõõdukas** | 10 -20 aasta tulemused | 4047 | LAGB  Vertical banded gastroplasty  RYGB  Konservatiivne  meetod | The  mean changes in body weight after 2,  10, 15, and 20 years were −23%,-17%, −16%, and −18% in the surgery group  and 0%, 1%, −1%, and −1% in the control group |
|  |  |  |  |  |
| Buddeberg  2006  Cohort study  **TK - Madal** | 3,2 aastat | 93 | LAGB  RYGB  Konservatiivne meetod | BMI at mean 3.2  years  34.9 (±5.5) 40.6 (±7.4)  P = 0.09  BMI change at  mean 3.2 years  -21.0 (±13.4) -5.5 (±11.1) P < 0.001  %excess weight loss  at mean 3.2 years  42.2 (±23.4) 11.5 (±25.8) P < 0.001 |
|  |  |  |  |  |
| Leslie et al.  2011  Vaatlusuuring  TK – Madal | 2 aastat | 267 | RYGB  Konservatiivne ravi | RYGB group had significantly greater %WL (mean ± 95% CI; 31.4±1.6% vs. −0.7±1.1%) and %EWL  (61.6±3.4% vs. −1.6±2.8%) at the 2-year time point (both  P<0.01) |
| Picot et al 2012  Süstemaatiline ülevaade, mis põhineb 2-l RCT-l  TK Mõõdukas | 2 aastat | 140 | LAGB  Konservatiivne ravi | Participants undergoing LAGB in the study  by Dixon et al. lost 62.5 % of their excess weight,  compared with just 4.3 % excess weight lost by those in the  non-surgery group. O’Brien et al. reported 87.2 %  of excess weight lost in participants with LAGB, while those in the non-surgical group lost 21.8 %, a statistically  significant difference. |

**Tabel 1b**

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| Autor/Aasta/  Uuringumeetod/  Tõendus-materjali kvaliteedi (TK) hinnang | Uuringu kestvus | Patsientide  arv | Ravimeetodid | Peamised tulemused |
| Mingrone et al. 2012  RCT  TK - Kõrge | 2 aastat | 60 | RYGB  BPD  Konservatiivne meetod | At 2 years, the average baseline  glycated hemoglobin level (8.65±1.45%) had decreased in all groups, but patients in the two surgical groups had the greatest degree of improvement (average glycated  hemoglobin levels, 7.69±0.57% in the medical-therapy group, 6.35±1.42% in the gastric-bypass group, and 4.95±0.49% in the biliopancreatic-diversion group)  At 2 years, diabetes remission had occurred in none of the patients receiving medical therapy, as compared with 15 of 20 (75%) undergoing gastric  bypass and 19 of 20 (95%) undergoing biliopancreatic  diversion (P<0.001 for both comparisons).  There was a significant association between study group and rate of remission |
| Sjöström et al.  2012  Mitte-randomiseeritud vaatlusuuring  TK - Mõõdukas | 10 aasta tulemused | 4047 | LAGB  Vertical banded gastroplasty  RYGB  Konservatiivne  meetod | Diabetes remission 35% in surgical and 11% in control group.  In a recent  update including data from all SOS subjects without  diabetes at baseline (1771 controls and 1658 in  the surgery group), bariatric surgery (as compared  with usual care) reduced the risk of developing T2D  by 96%, 84% and 78% after 2, 10 and 15 years  respectively |
| Picot et al 2012  Süstemaatiline ülevaade, mis põhineb 2-l RCT-l  TK Mõõdukas | 2 aastat | 140 | LAGB  Konservatiivne ravi | After 2 years, over 70 % of participants in the LAGB group experienced remission of their T2D, whereas in the non-surgical group only 13 % had  T2D remission (p<0.001). LAGB was also associated with a statistically significant reduction in the proportion of participants with metabolic syndrome in both the included  studies. |
| Leslie et al.  2011  Vaatlusuuring  TK – Madal | 2 aastat | 267 | RYGB  Konservatiivne ravi | HbA1C in the RYGB cohort was significantly lower than the RMM group at 2 years (6.4±  0.1 vs. 7.2±0.1, P<0.01). No significant change in mean HbA1C was observed in the RMM group over the 2-year  observation period, but there was a significant decrease in  HbA1C in the RYGB group (P<0.01). |
| Kwok et al 2014  Metaanalüüs  TK - Kõrge | 2 – 14,7 aastat | 29208  vs  166200 | Kirurgiline ravi  Konservatiivne ravi | Compared to nonsurgical controls there was more than 50% reduction in mortality amongst  patients who had bariatric surgery (OR 0.48 95% CI 0.35–0.64, I2 = 86%, 14 studies). In pooled analysis of four  studieswith adjusted data, bariatric surgerywas associatedwith a significantly reduced risk of composite cardiovascular  adverse events (OR 0.54 95% CI 0.41–0.70, I2 = 58%). Bariatric surgery was also associated with significant  reduction in specific endpoints of myocardial infarction (OR 0.46 95% CI 0.30–0.69, I2=79%, 4 studies) and  stroke (OR 0.49 95% CI 0.32–0.75, I2 = 59%, 4 studies). |

**Tabel 1c**

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| Autor/Aasta/  Uuringumeetod/  Tõendus-materjali kvaliteedi (TK) hinnang | Uuringu kestvus | Patsientide  arv | Ravimeetodid | Peamised tulemused |
| Picot et al 2012  Süstemaatiline ülevaade, mis põhineb 2-l RCT-l  TK Mõõdukas | 2 aastat | 140 | LAGB  Konservatiivne ravi | LAGB costs  more than non-surgical management. For people with class I or II obesity and type 2 diabetes (T2D), the incremental costeffectiveness  ratio (ICER) at 2 years is £20,159, reducing to  £4,969 at 5 years and £1,634 at 20 years. Resolution of T2D makes the greatest contribution to this reduction. In people with class I obesity, the ICER is £63,156 at 2 years, £17,158 at  5 years, and £13,701 at 20 years. Cost-effectiveness results are particularly sensitive to utility gain from reduction in BMI,  factors associated with poorer surgical performance and diabetes  health state costs.  Surgical management is more costly but also results in improved  outcomes (in terms of quality-adjusted life years [QALYs]) over  each of the modelled time horizons |
| Padwal et al.  2011  Süstemaatiline ülevaade  TK- Kõrge |  |  |  | Surgery resulted in long-term incremental cost–utility ratios of $ <1.000–  $40,000 (2009 USD) per quality-adjusted-life-year compared  with non-surgical treatment. |
| O´Brien  2006  RCT  **TK – Kõrge** | 2 aastat | 60 | LAGB  Konservatiivne ravi | Study compared changes in the short form health survey  (SF-36) domain scores from baseline to two years follow-up for people undergoing laparoscopic adjustable gastric banding and  non-surgical therapy. Although no point estimates were reported,  the authors noted improvements in scores on all eight domains  for the laparoscopic adjustable gastric banding group and on three  domains (physical function, vitality and mental health) for the  non-surgical therapy group. Statistically significantly greater improvements  were reported for five of the eight domains for laparoscopic  adjustable gastric banding compared to the non-surgical  group |
| Karlsson et al.  2007  Mitte-randomiseeritud vaatlusuuring  TK - Mõõdukas | 10 aasta tulemused | 4047 | LAGB  Vertical banded gastroplasty  RYGB  Konservatiivne  meetod | After 10  years follow-up, the mean level of current health perception, social  interaction, obesity-related problems, overall mood, and depression  did not differ significantly between the surgery and conventional  treatment groups, although the surgery group had more  anxiety (P < 0.01). However, statistically significantly greater 10-  year change was observed in the surgery group for current health  perceptions, social interaction, obesity-related problems and depression.  There was no statistically significant difference in 10-  year change for overall mood and anxiety |
| Buddeberg  2006  Cohort study  **TK - Madal** | 3,2 aastat | 93 | LAGB  RYGB  Konservatiivne meetod | Three-quarters of the patients who had undergone bariatric surgery and two-thirds of the no-surgery group rated their physical and mental health as “good”. There was no significant  difference between the two groups, although more patients in the bariatric surgery group assessed  their level of satisfaction as “good” |
| Canetti et al. 2013  Vaatlusuuring  **TK- Madal** | 1 aasta | 97 | LAGB  Konservatiivne ravi | After  one year, the surgery group showed higher scores than the community norm in all SF-36 scales:  physical functioning, role physical, bodily pain,  health perception, vitality, social functioning, role  emotional, and mental health (t(2,072) = -4.86,  p < .001, t(2,072) = -3.55, p < .001, t(2,072) =  -1.65, p < .05 one-tailed, t(2,072) = -5.63, p < .001,  t(2,072) = - 3.36, p < .01, t(2,072) = -2.73, p < .01,  t(2,072) = -2.38, p < .02, and t(2,072) = -3.78, p <  .001, respectively). |
| Sjöström 2004  Mitterandomiseeritud vaatlusuuring  **TK- Mõõdukas** | 10 | 1703 | Adjustable gastric bandind  Vertical banded gastroplasty  RYGB  Konservatiivne ravi | Similarly,the fraction of subjects physically active during leisure time was higher in the surgery group over the 10-year period, and the fraction of those physically active during work time was higher in the surgery group for the first 6 years of the intervention |
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|  |  |  |  |  |
| Mäklin et al  2011  Süstemaatiline ülevaade  **TK - Kõrge** |  |  |  | The reduction in annual healthcare costs reached the costs of bariatric surgery on average in about 5 years (5 years for gastric bypass and sleeve gastrectomy, 6 years for gastric  banding). The expected  healthcare costs of patients having ordinary treatment  were about 1·5 times higher than the corresponding  costs of bariatric surgery, using the 10-year time horizon |
| **Skubleny et al 2015**  **Metaanalüüs**  **TK Mõõdukas** |  | 2130 |  | The incidence of PCOS preoperatively was 45.6 %, which significantly decreased to 6.8 % (P<0.001) and 7.1 % (P<0.0002) at 12-month follow-up and  study endpoint (Fig. 3), respectively. 56.2 % of patients reportedpreoperative menstrual irregularity which  improved significantly following surgery, with the incidence  decreasing to 7.7%(P<0.0001) and 7.1 %(P<0.00001) at 12-month follow-up and study endpoint respectively.  The incidence of hirsutism preoperatively was 67.0 % which decreased significantly postoperatively to  38.6 % at 12-month follow-up (P=0.03) and further to  32.0 % at study end (P<0.0002) The incidence of  preoperative infertility was 18.2 % which significantly  decreased to 4.3%at study end P=0.0009) Of note, heterogeneity was significant for all outcomes, except  for infertility. |