

Aktuelle Therapie des Barrettkarzinoms

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UniversitätsSpital
Zürich

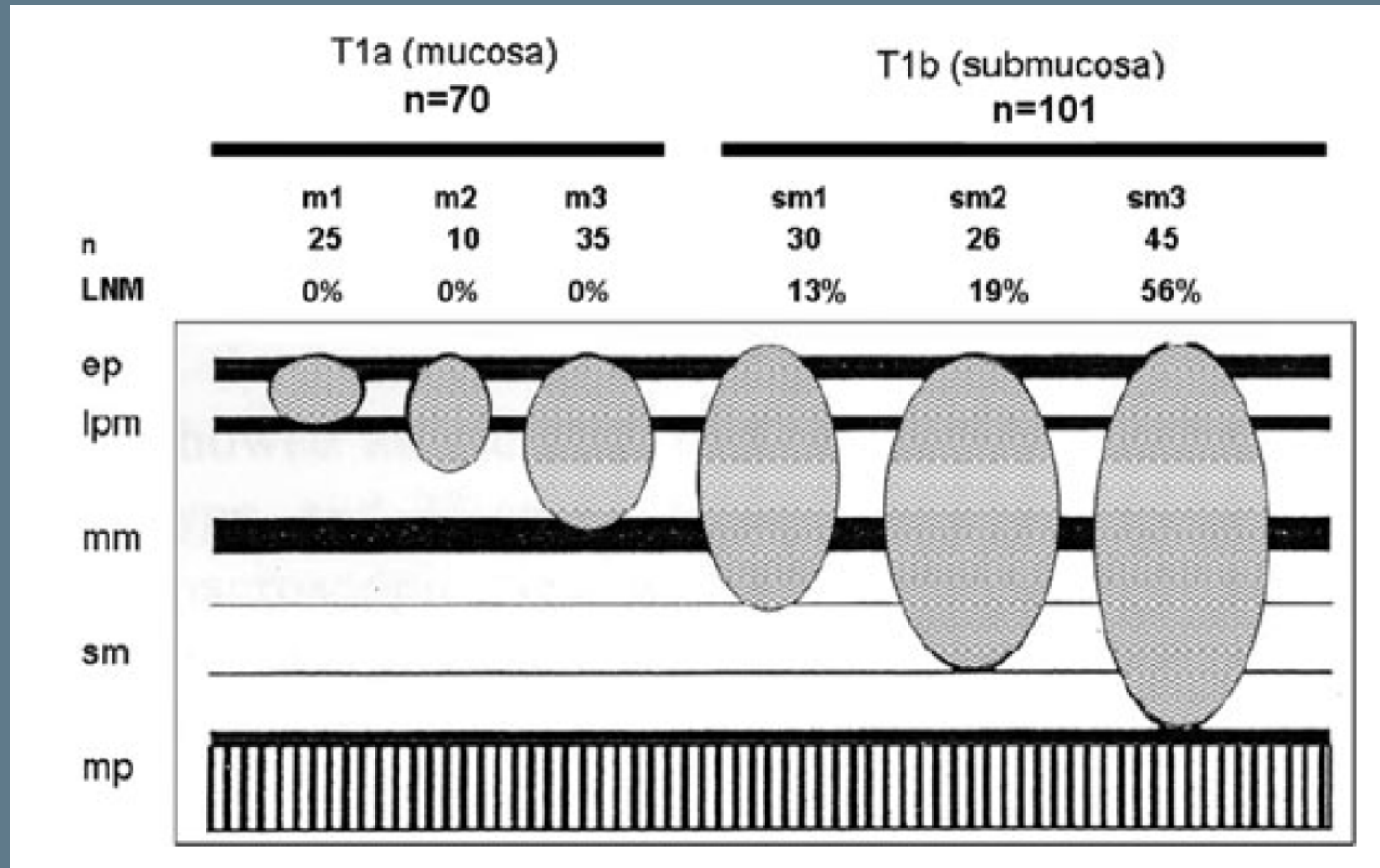


Therapeutische Konzepte - Übersicht

Stadium	Therapie
Intestinale Metaplasie ohne Dysplasie Low-Grade Dysplasie (LGIEN)	Surveillance Endoskopische Ablation
High-Grade Dysplasie (HGIEN) Frühkarzinom vom Mukosatyp (m1-4)	Endoskopische Ablation Endoskopische Resektion Chirurgische Resektion
Frühkarzinom vom Submukosa-Typ (sm1-3)	sm1: Endoskopische Resektion (G1-2) sm2-3: Chirurgische Resektion
cT2 N0 M0	Chirurgische Resektion Multimodale Therapie
cT3-4 Nx M0	Multimodale Therapie

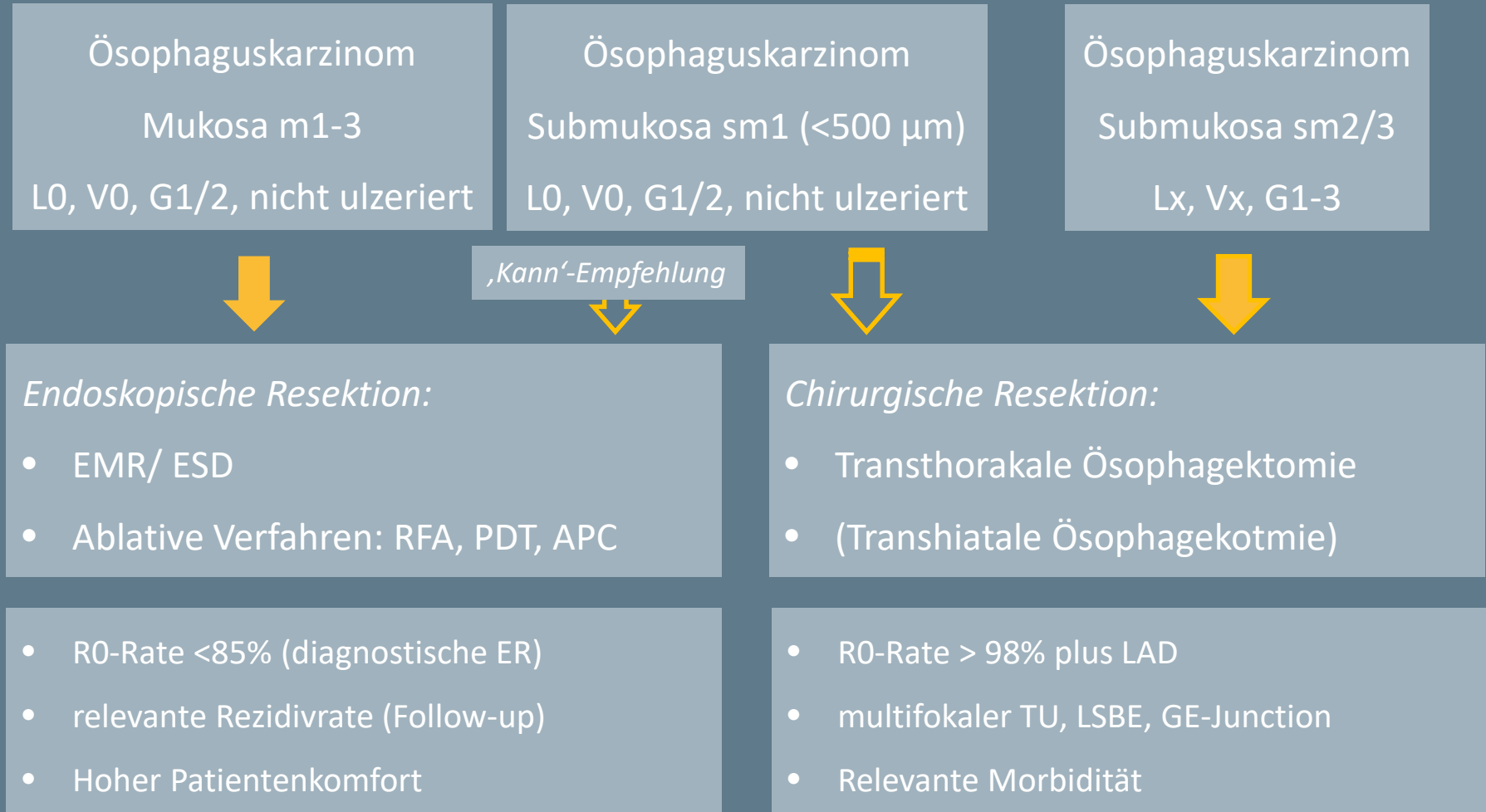
Ösophagusfrühkarzinome

Lymphknotenmetastasierung:



Hölscher/Schröder/Gutschow, Ann Surg 2011, 254 (5): 801

Barrett-Frühkarzinome – Standards 2019



Lokal fortgeschrittenes Barrett-Karzinom – Standards 2019

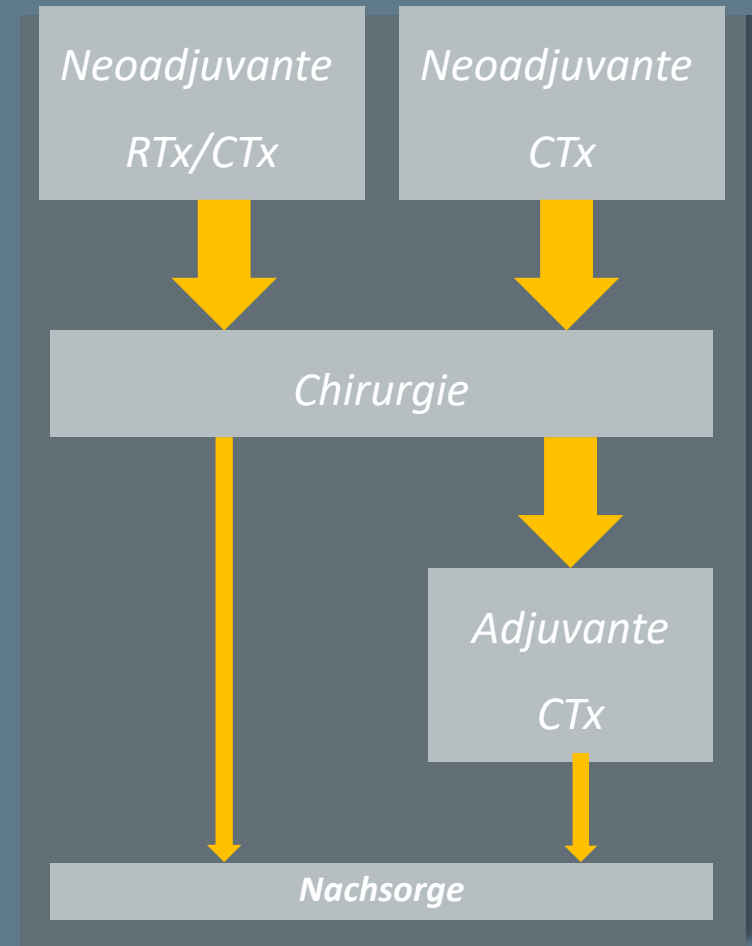
Multimodale Therapie für AC, cT2-4 M0:

Neoadjuvante Radiochemotherapie:

- CROSS-Protokoll (41.4Gy, Paclitaxel, Carboplatin)

Perioperative Chemotherapie:

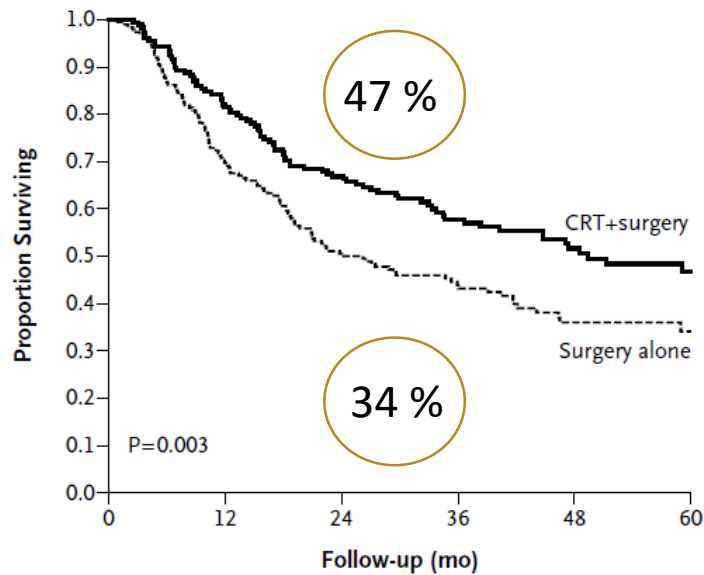
- FLOT (Docetacel, Oxaliplatin, Fluorouracil, Leucovorin)
- ECF (Epirubicin, Cisplatin, Fluorouracil)



CROSS-Protokoll

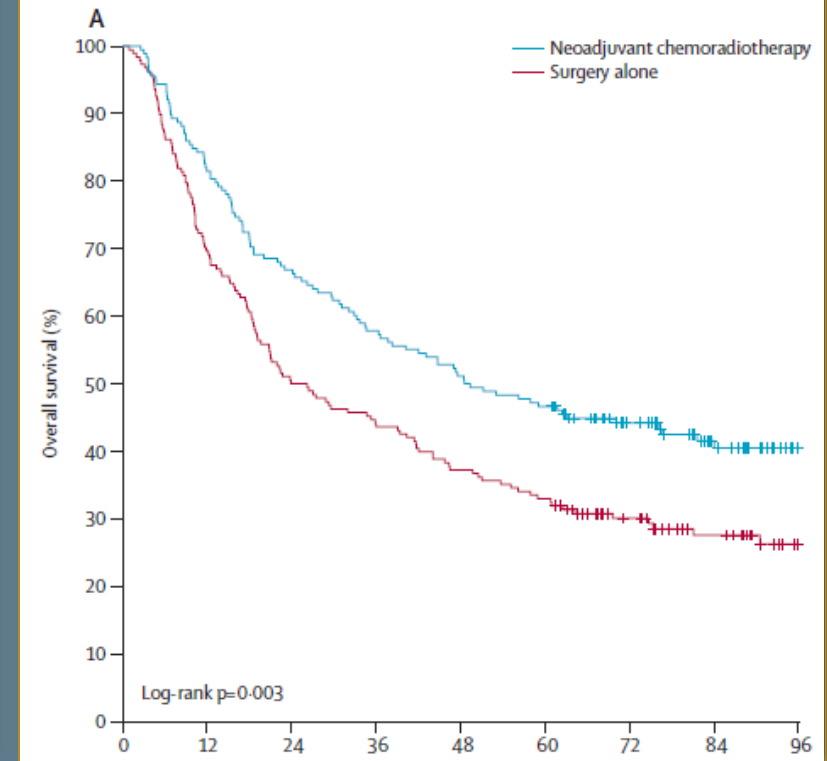
(5 Wochen Radiochemotherapie: 41.4Gy, Paclitaxel, Carboplatin)

A Survival According to Treatment Group



No. at Risk

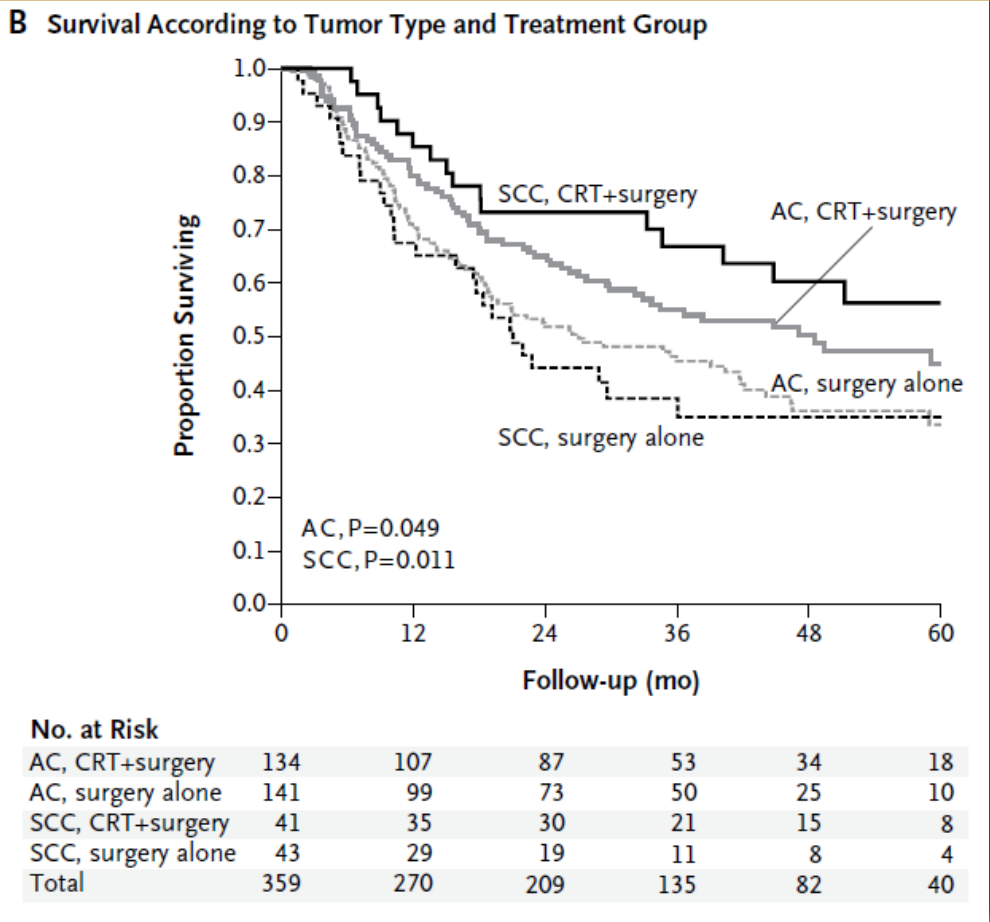
	0	12	24	36	48	60
CRT+surgery	178	145	119	75	49	28
Surgery alone	188	131	94	62	33	17
Total	366	276	213	137	82	45



Van Hagen, NEJM 2012, 366(22): 207

Shapiro, Lancet Oncol 2015, 16:1090 4

CROSS-Protokoll



„Pathological complete response’
(pCR):

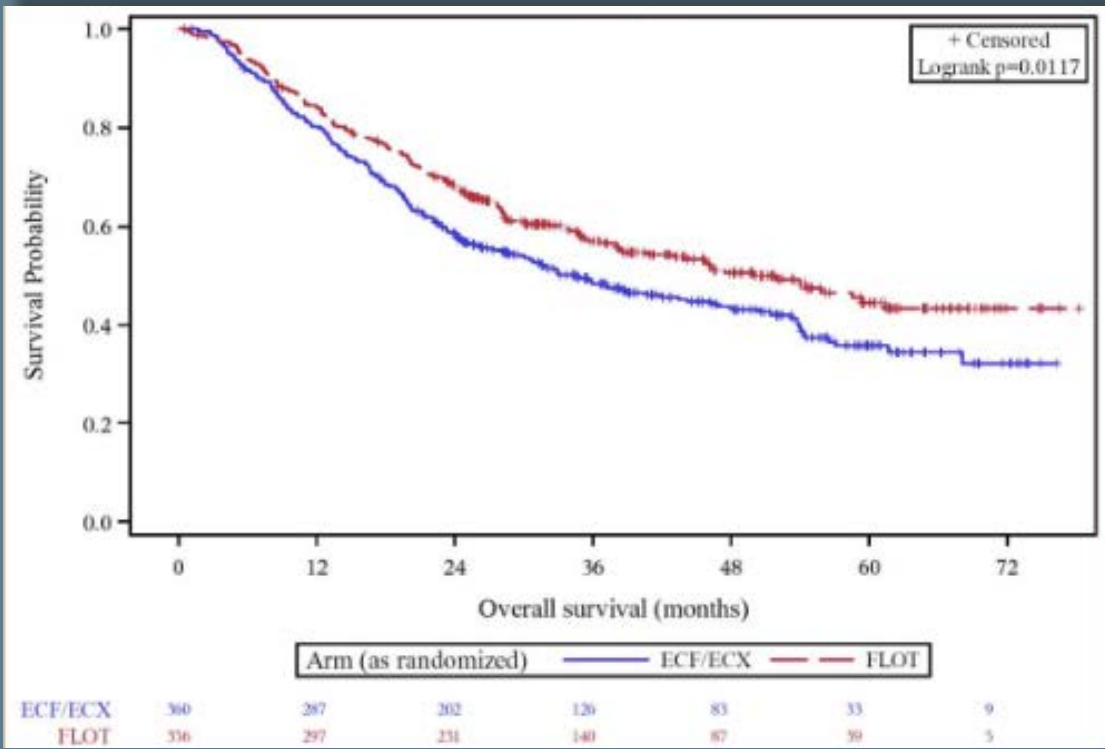
- AC 28/121 patients (23%)
- SCC 18/37 patients (49%)

P = 0.008

FLOT-4-AIO Trial: ECF (MAGIC-Trial) vs FLOT

	ECF/ECX (n=137)	95% CI	FLOT (n=128)	95% CI	p value*
Complete (TRG 1a)†	8 (6%)	2.8–11.3%	20 (16%)	10.3–23.0%	0.02
Subtotal (TRG 1b)	23 (17%)	11.4–24.0%	27 (21%)	14.9–29.0%	..
Complete or subtotal (TRG 1a/b)	31 (23%)	16.4–30.4%	47 (37%)	28.9–45.4%	0.02
Partial (TRG 2)	28 (20%)	14.5–28.0%	23 (18%)	12.2–25.6%	..
Minimal or none (TRG 3)	52 (38%)	30.3–46.3%	49 (38%)	30.3–46.9%	..
No surgery	26 (19%)	13.2–26.4%	9 (7%)	3.6–13.0%	..

FLOT-4-AIO Trial: ECF (MAGIC-Trial) vs FLOT



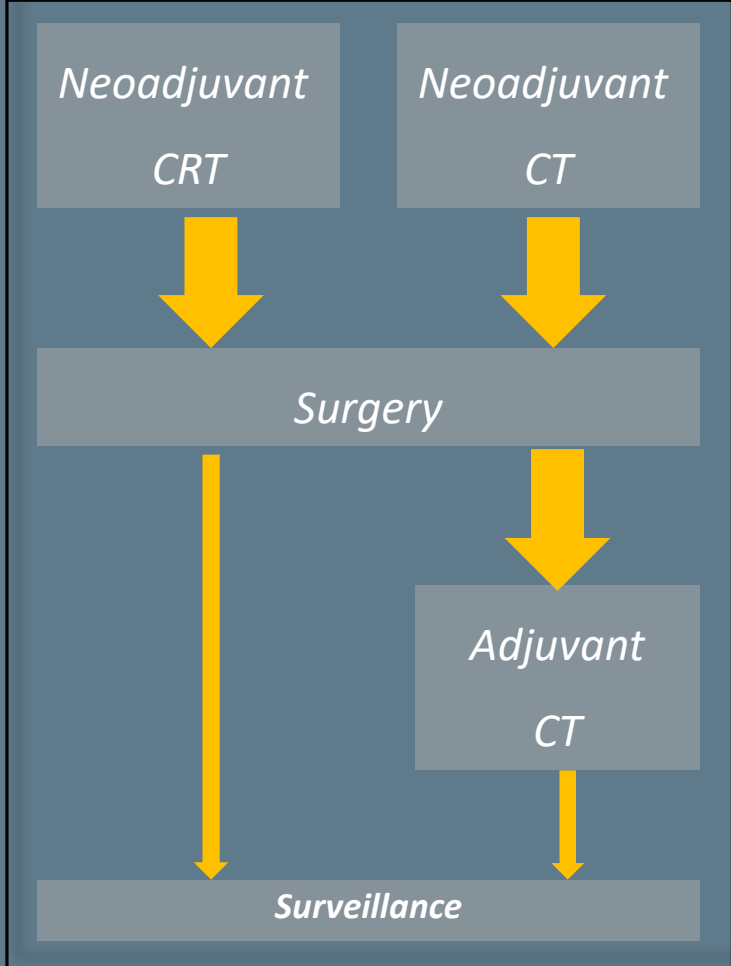
	ECF/ECX	FLOT
mOS months	35 months	50
	[27-46]	[38-na]
HR	0.77 [0.63 - 0.94] p=0.012 (log rank)	
OS rate*	ECF/ECX	FLOT
2y		59%
3y		68%
5y		48%
Projected OS rates		57%
		36%
		45%

Al-Batran et al., ASCO 2017

Onkologische Standards

Multimodale Therapie für AC, cT2-4 M0:

- Neoadjuvante RTx/CTx: CROSS
- oder:
- Perioperative CTx: FLOT



Hoepfner et al. *BMC Cancer* (2016) 16:503
DOI 10.1186/s12885-016-2564-y

BMC Cancer

STUDY PROTOCOL Open Access

ESOPEC: prospective randomized controlled multicenter phase III trial comparing perioperative chemotherapy (FLOT protocol) to neoadjuvant chemoradiation (CROSS protocol) in patients with adenocarcinoma of the esophagus (NCT02509286)

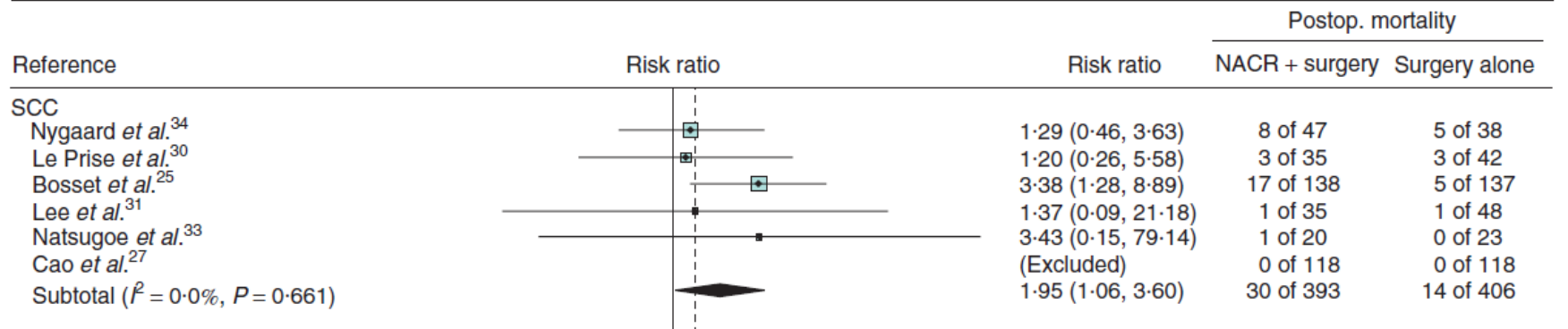
Jens Hoepfner^{1*}, Florian Lordick², Thomas Brunner³, Torben Glatz¹, Peter Bronsert⁴, Nadine Röthling⁵, Claudia Schmoor⁵, Dietmar Lorenz⁶, Christian Ell⁷, Ulrich T. Hopt¹ and J. Rüdiger Siewert⁸

*Correspondence: jens.hoepfner@klinik.uni-wuerzburg.de

Multimodale Therapie und perioperative Morbidität/Mortalität

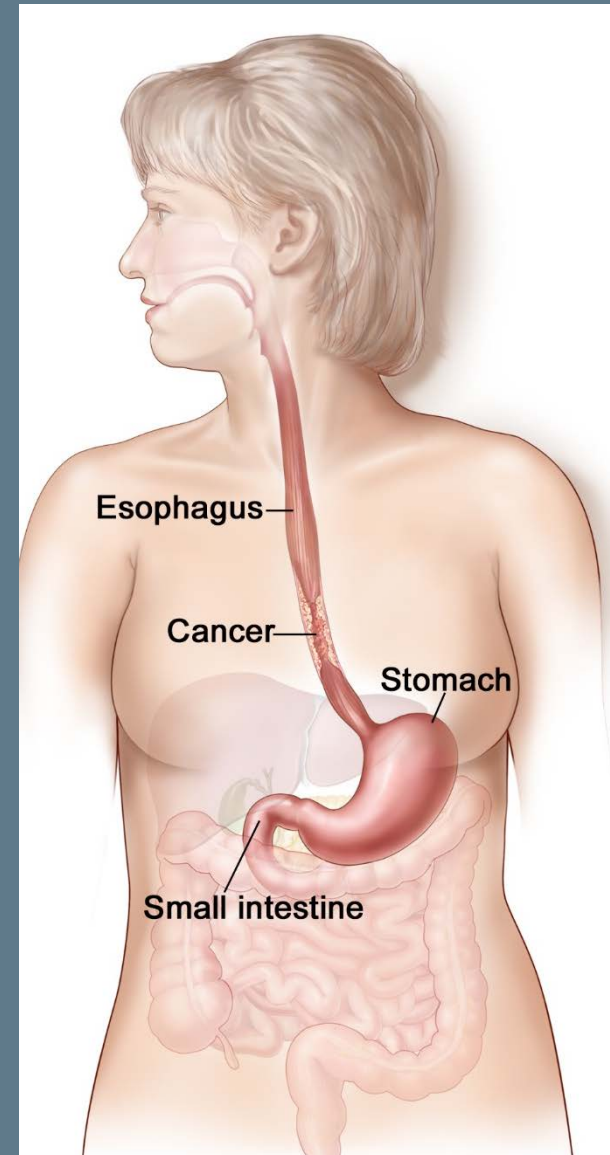
Metaanalyse, 23 prospektive Studien:

- Neoadjuvante CTx und RTx/CTx erhöhen nicht periop. Morbidität/Mortalität
- Kein Unterschied der periop. Morbidität/Mortalität zwischen CTx und RTx/CTx
- Subgruppenanalyse: Mortalität nach neoadjuvanter RTx/CTx bei SCC erhöht

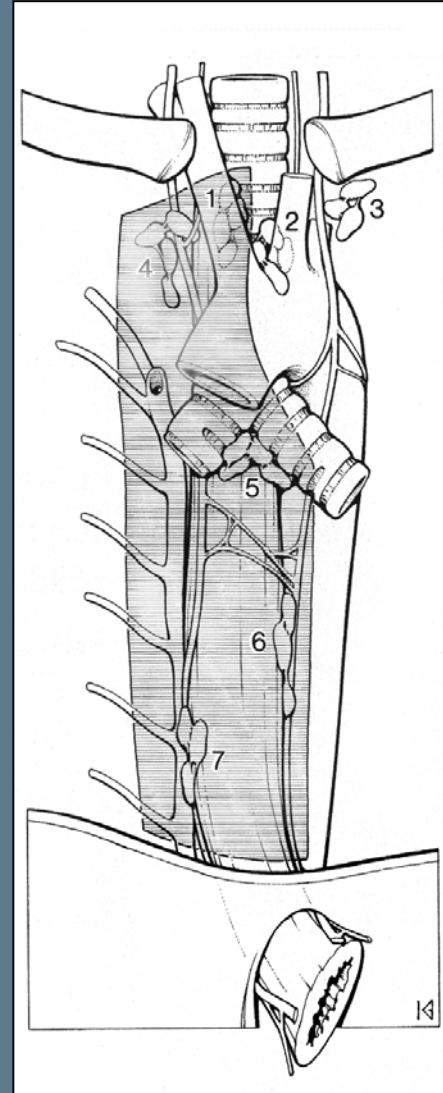


Chirurgische Standardverfahren

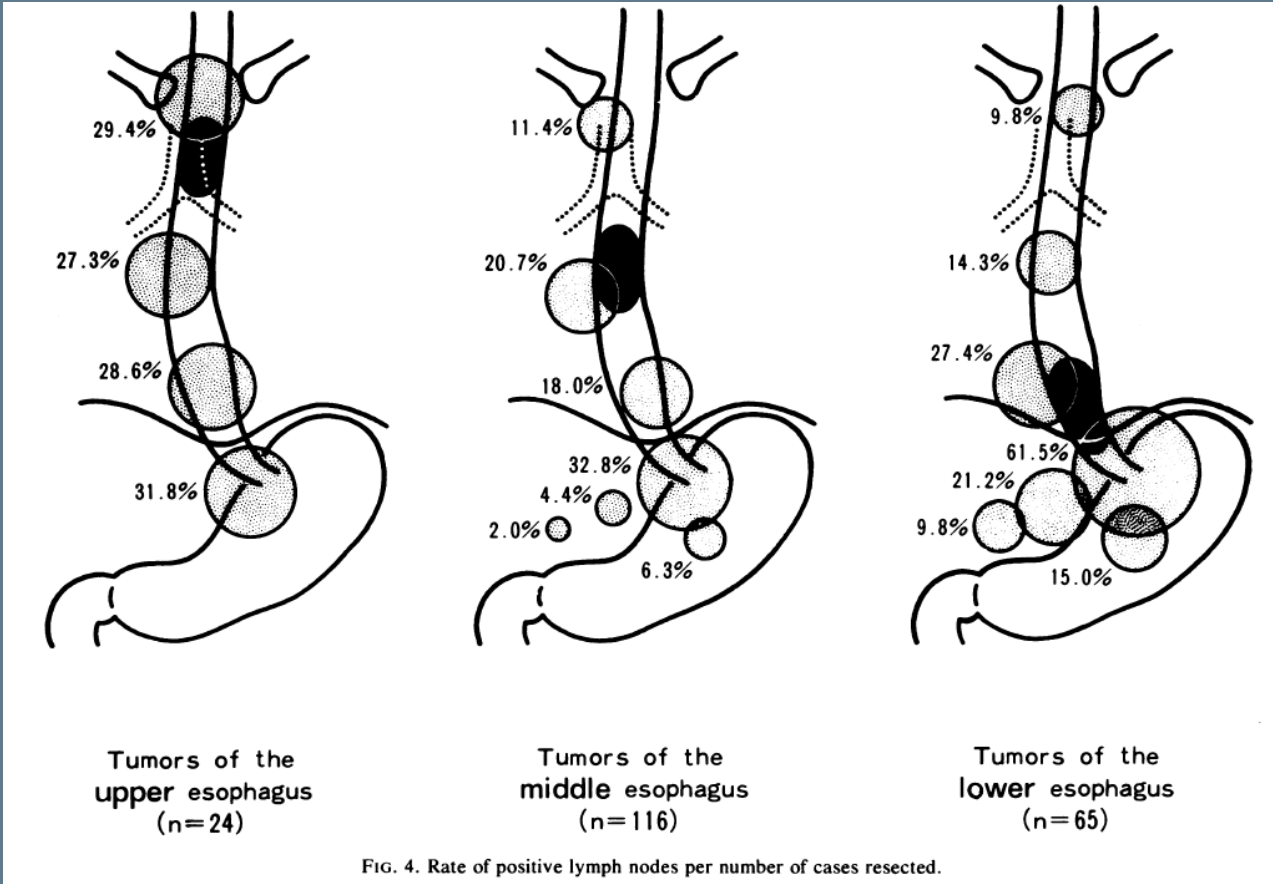
- Transthorakale Ösophagektomie mit 2-Feld (3-Feld) LAD
- (Transhiatale Ösophagektomie)
- Rekonstruktion durch Magenhochzug
 - mit hoch-intrathorakaler Anastomose (Ivor Lewis)
 - mit zervikaler Anastomose (McKeown)
- (Rekonstruktion durch Kolon-/Jejunuminterposition)

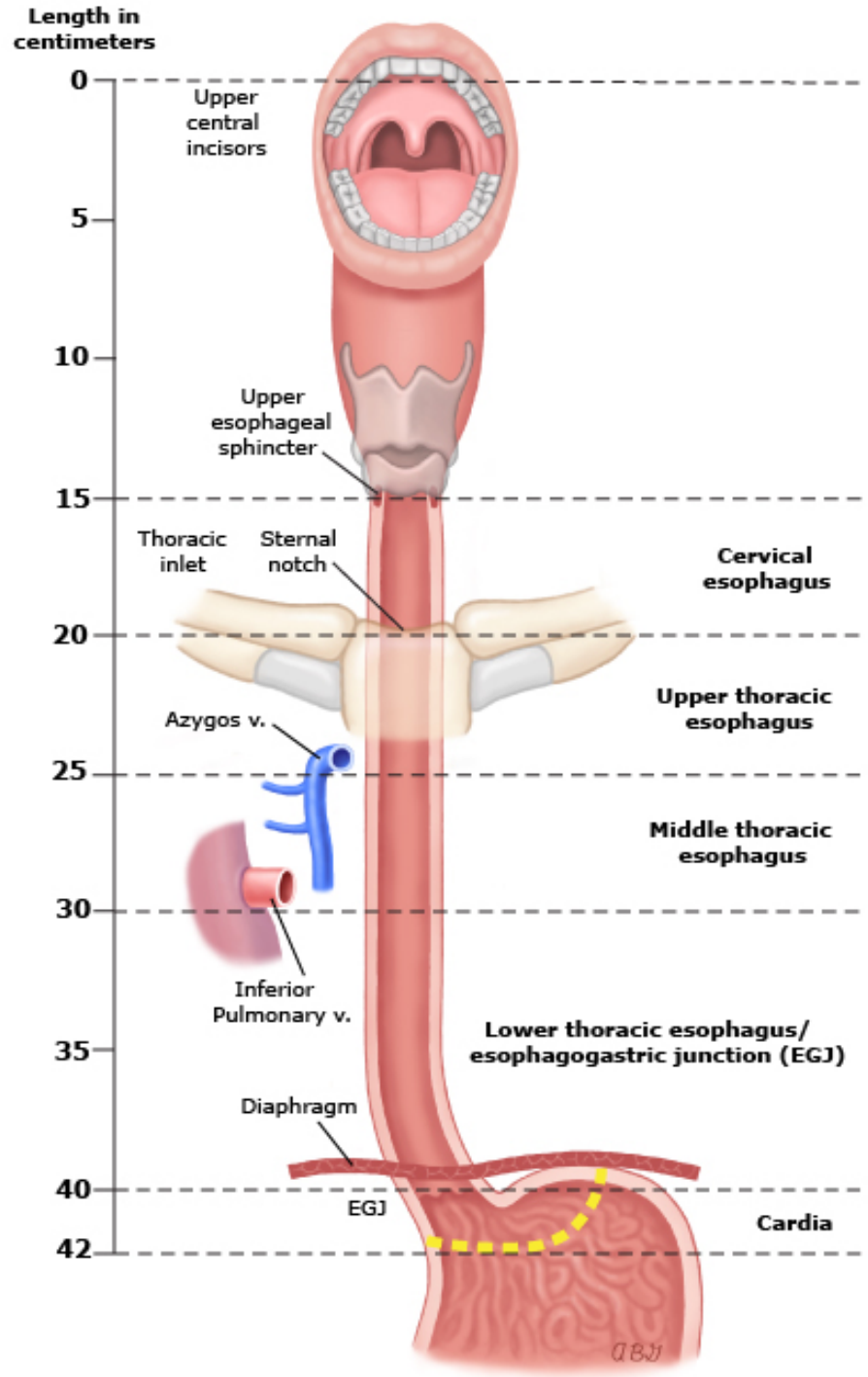


Resektionsausmass



Bidirektionale Lymphknotenmetastasierung





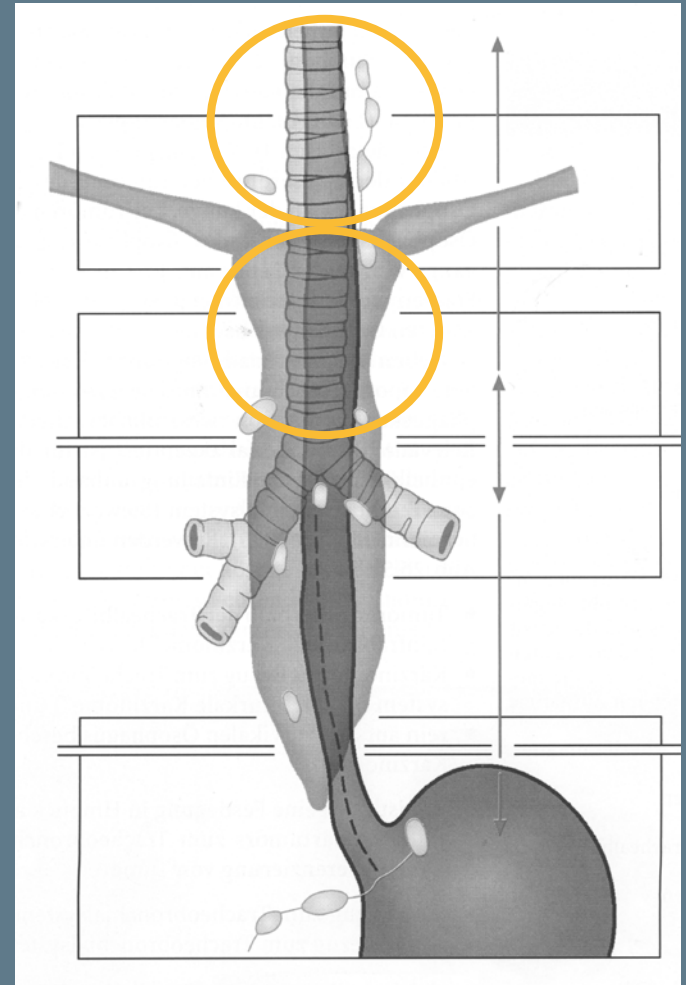
McKeown Ösophagektomie

Ivor Lewis Ösophagektomie



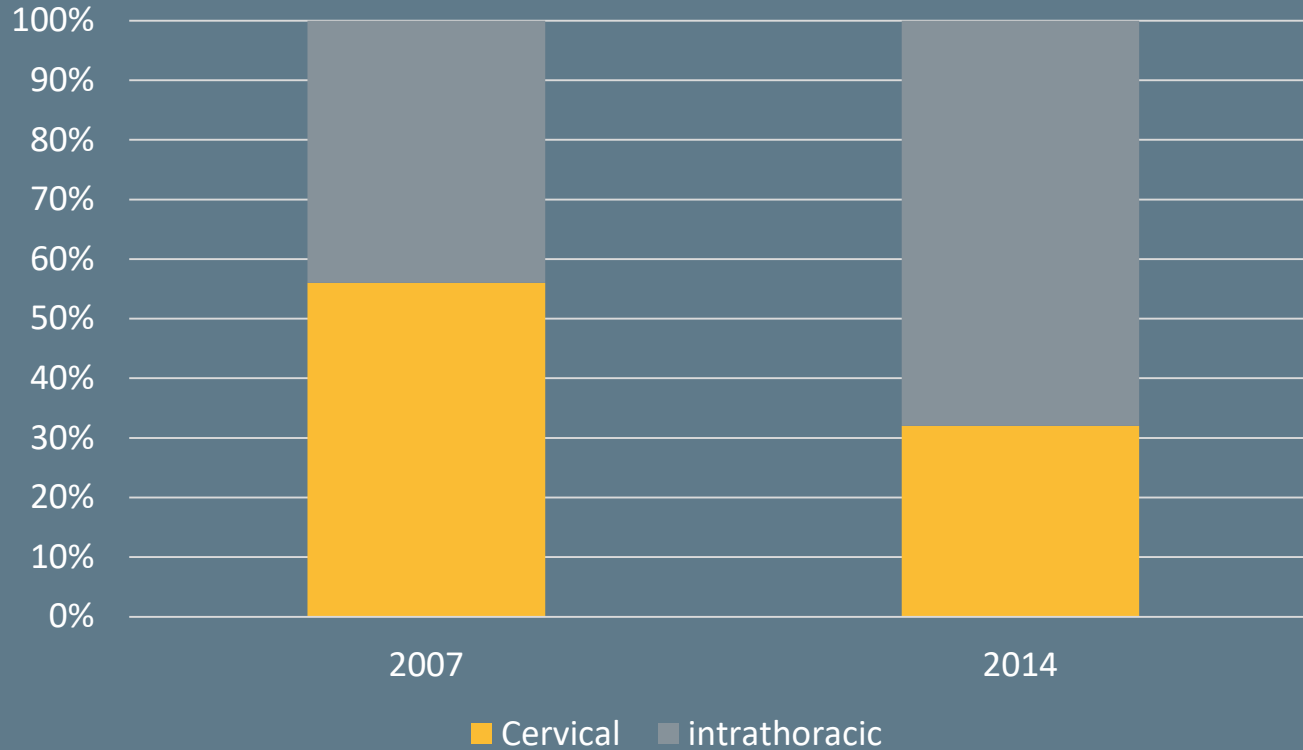
Intrathorakale vs. zervikale Anastomose

- 3x höhere Insuffizienzrate der zervikalen Anastomose
- 5x höhere Strikturrate der zervikalen Anastomose
- bessere Schluckfunktion der intrathorakalen Anastomose



Transthorakale Ösophagektomie

Internationale Umfrage: 478 Chirurgen, 79 Länder, 6 Kontinente



Technische Entwicklung Ösophagektomie

Transthorakale OE/MHZ, McKeown



Transthorakale OE/MHZ, Ivor Lewis



Hybrid OE/MHZ, Ivor Lewis



Total minimal-invasive OE/MHZ, Ivor Lewis



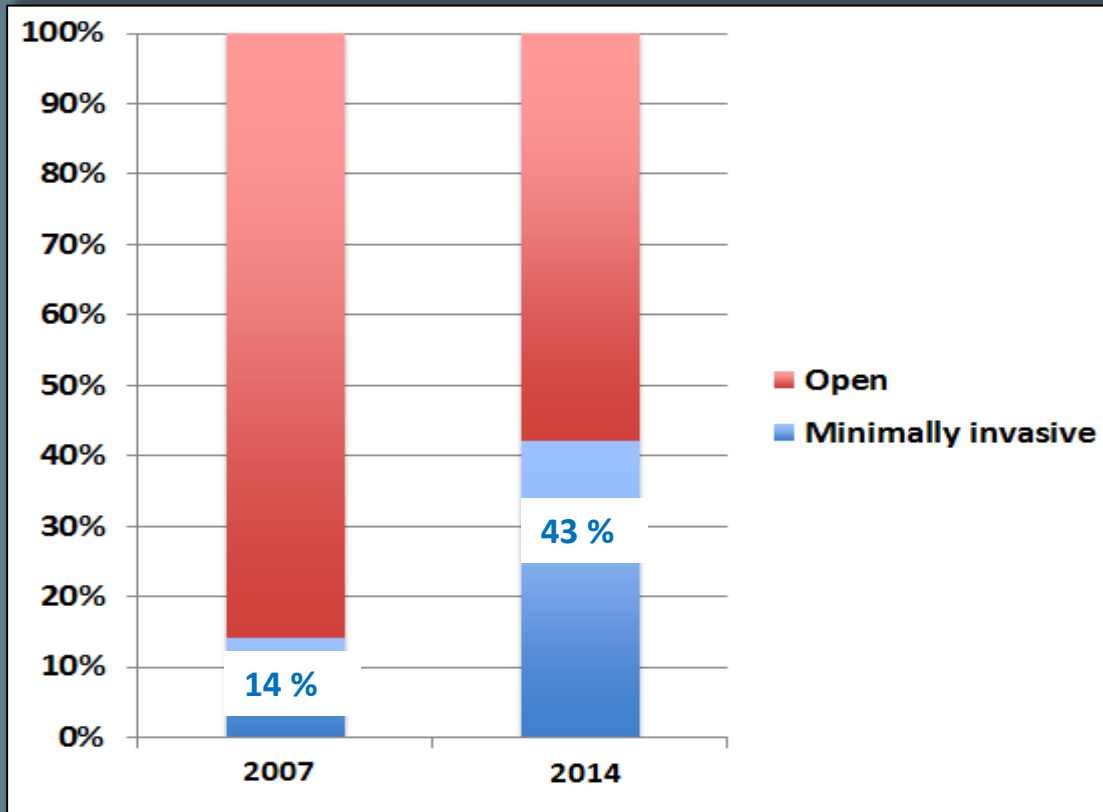
Roboter-assistierte OE/MHZ, Ivor Lewis

Standard ,S3-Leitlinie'

MIC Ösophagektomie

Minimal-invasive Ösophagektomie

Internationale Umfrage: 478 Chirurgen, 79 Länder, 6 Kontinente

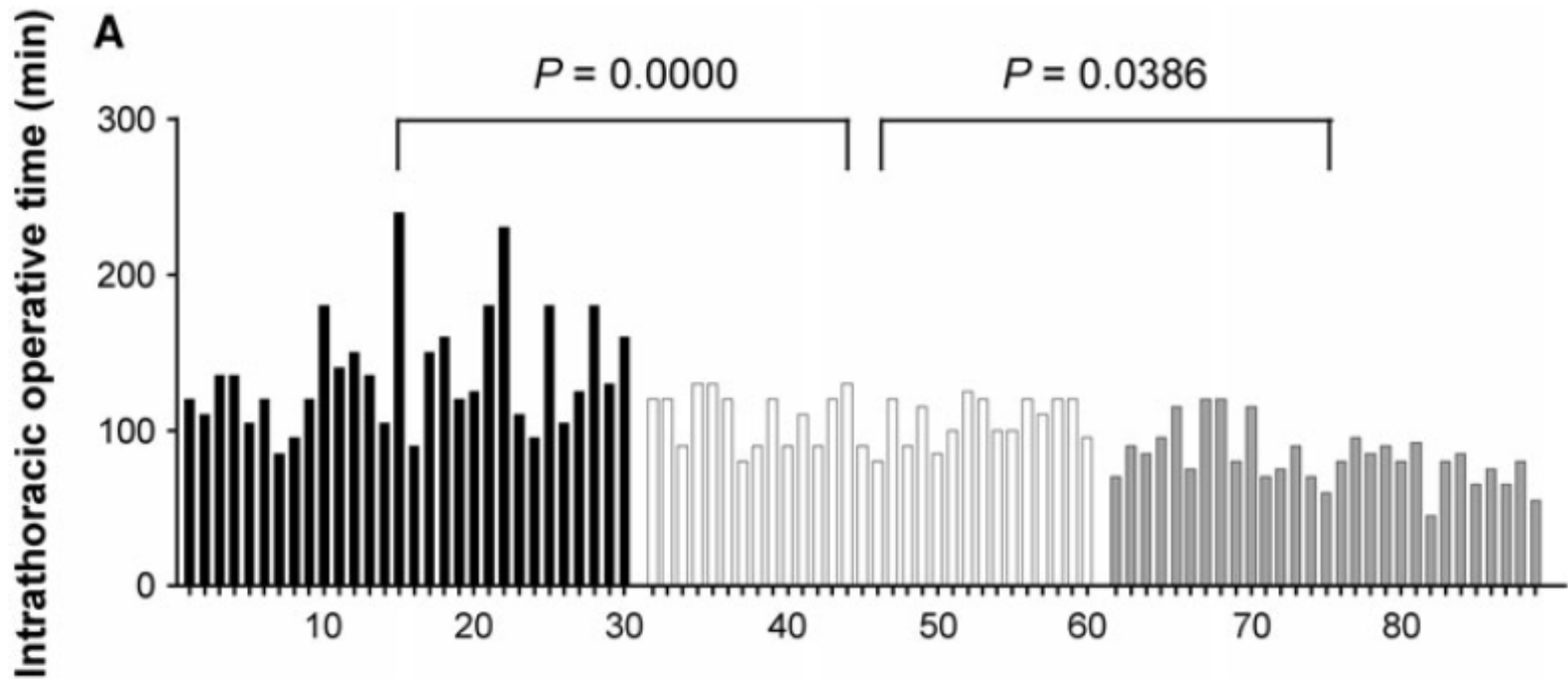


Studienlage

Prospektive randomisierte Studien (EBM IB) – Stand 2019

Trial	Country	Study Design	N	Status
TIME-Trial	Netherland	Open OE vs ttMIE	115	Published <i>(Lancet 2012, Ann Surg 2017)</i>
MIRO-Trial	France	Open OE vs hybrid MIE	207	ASCO 2014 Published <i>(NEJM 2019)</i>
ROBOT-Trial	Netherland	Open OE vs robotic MIE	109	Published <i>(Ann Surg 2018)</i>
ROMIO-Trial	UK	Open OE vs hybrid vs ttMIE	106	Pilot study <i>(Health Tech Ass 2016)</i> Recruiting
JCOG 1409 Trial	Japan	Open OE vs ttMIE	300	Recruiting

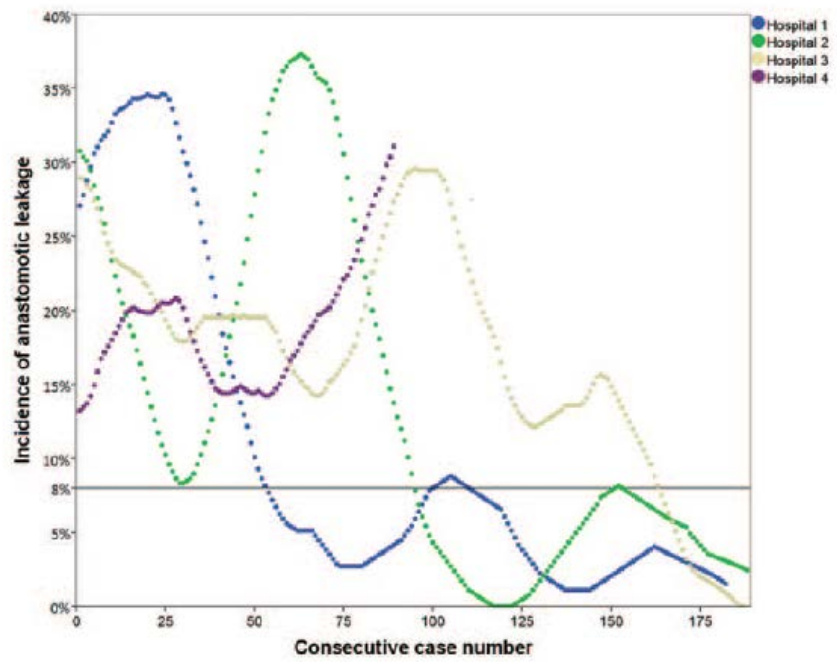
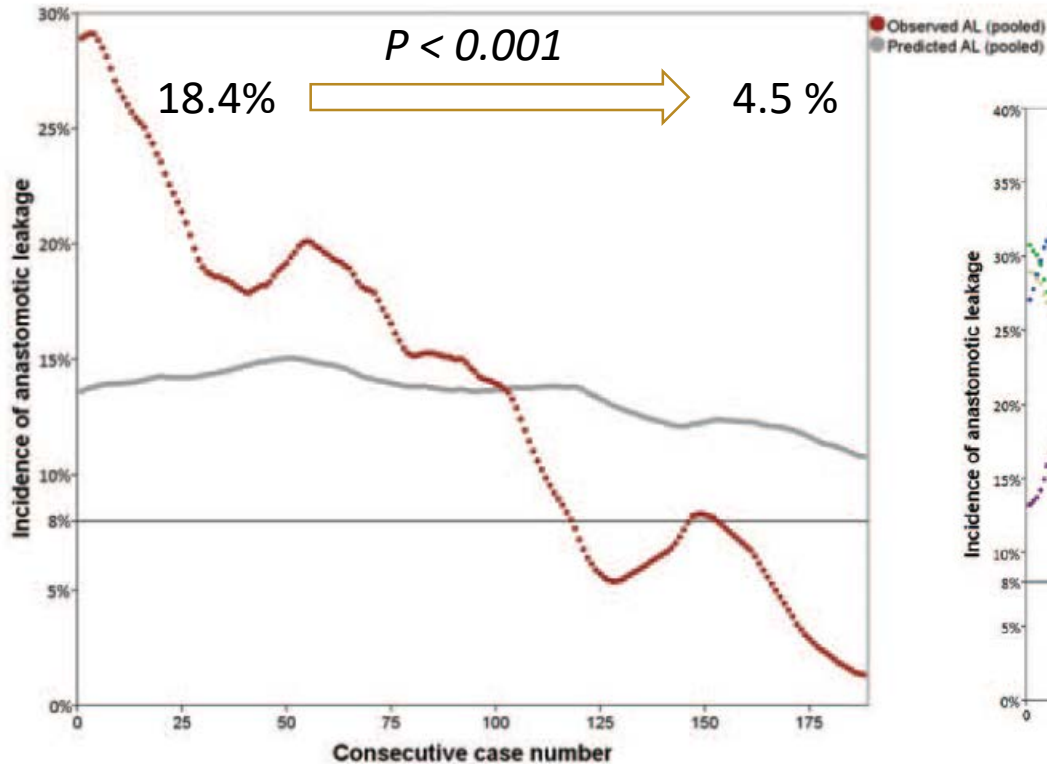
One surgeon's learning curve for video-assisted thoracoscopic esophagectomy for esophageal cancer with the patient in lateral position: how many cases are needed to reach competence?



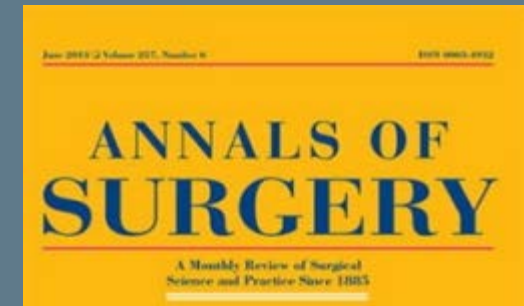
Lernkurve MIC Ösophagektomie

Retrospektive Analyse: 4 High-Volumen Zentren, 646 ttMIE (Ivor Lewis)

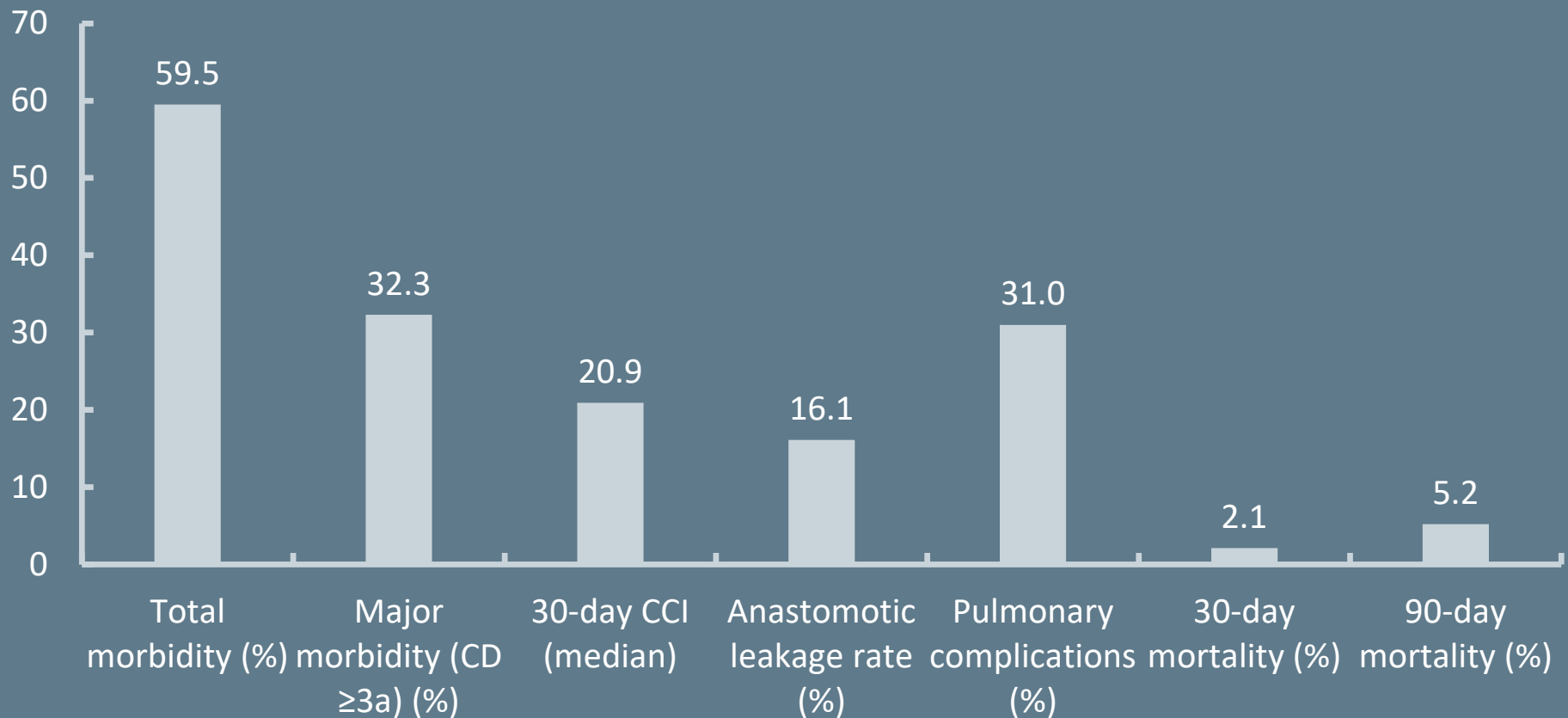
Zielparameter: Insuffizienzrate



Defining Benchmarks for Transthoracic Esophagectomy

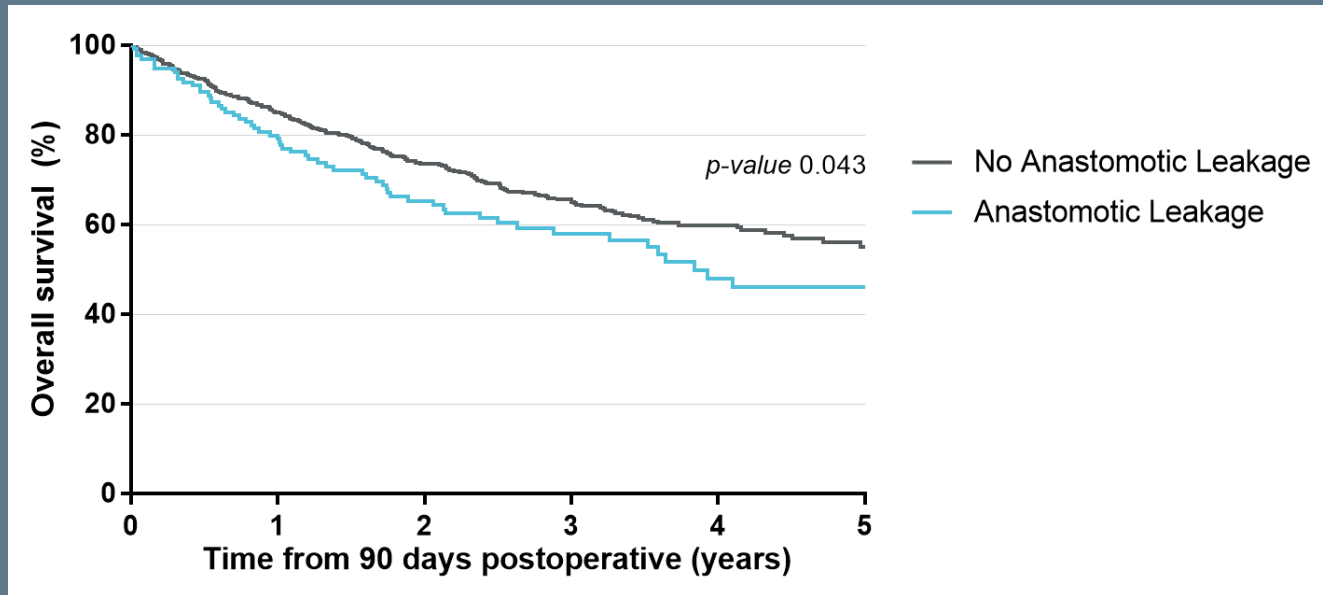


Retrospektive Analyse: 13 High-Volumen Zentren, 1057 ttMIE (IL und McKeown)



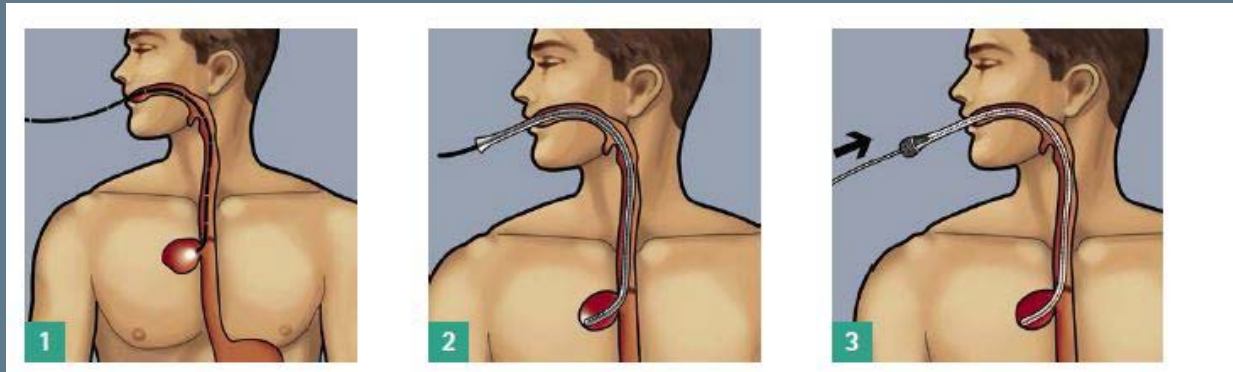
Schmidt, Gutschow *Ann Surg* 2017

EsoBenchmark Spin-off Projekt: Effect of anastomotic leakage on overall survival



Preemptive endoluminal vacuum therapy to reduce anastomotic leakage after esophagectomy: a game-changing approach?

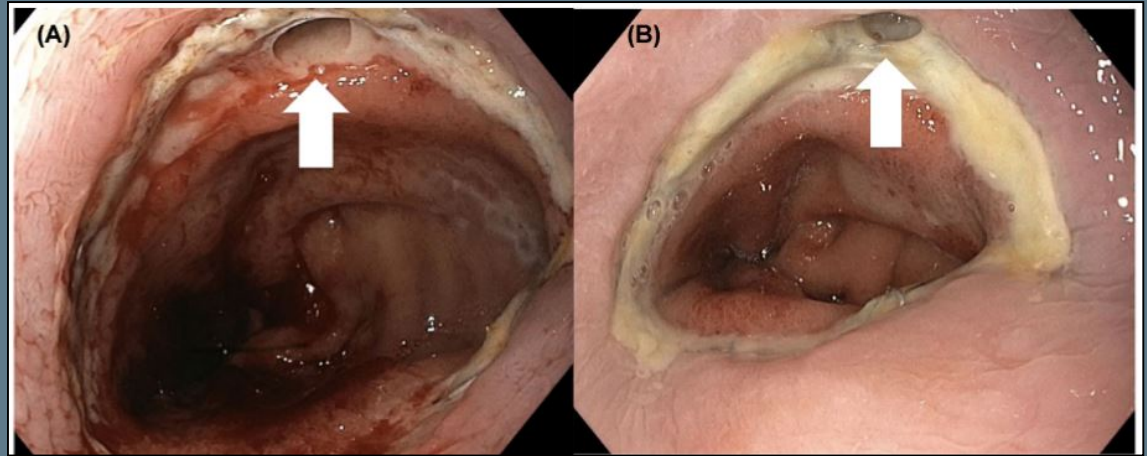
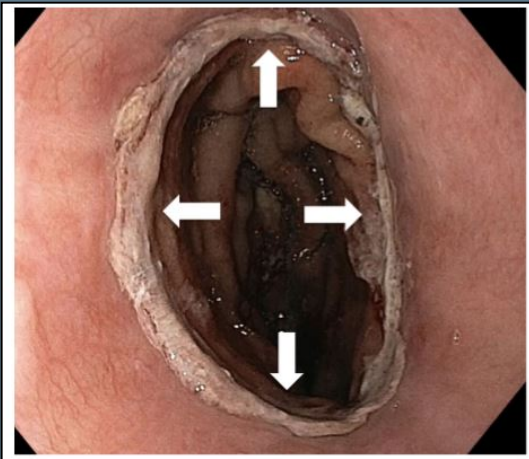
C. Gubler,¹ D. Vetter,² H. M. Schmidt,² P. C. Müller,² B. Morell,¹ D. Raptis,³ C. A. Gutschow²



Preemptive endoluminal vacuum therapy to reduce anastomotic leakage after esophagectomy: a game-changing approach?

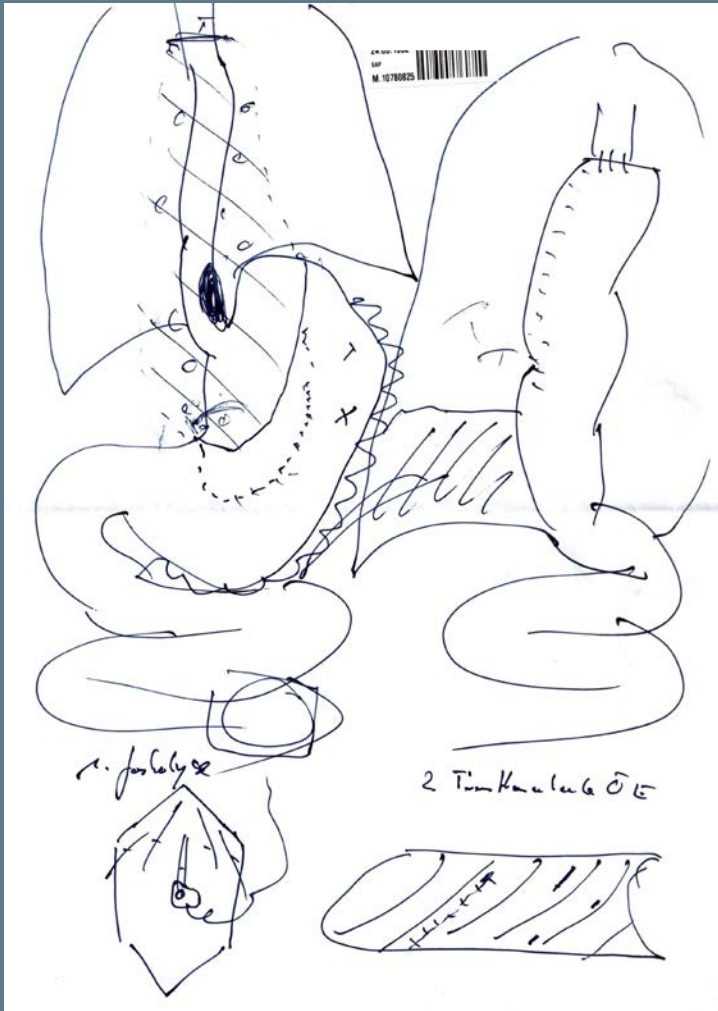
C. Gubler,¹ D. Vetter,² H. M. Schmidt,² P. C. Müller,² B. Morell,¹ D. Raptis,³ C. A. Gutschow²

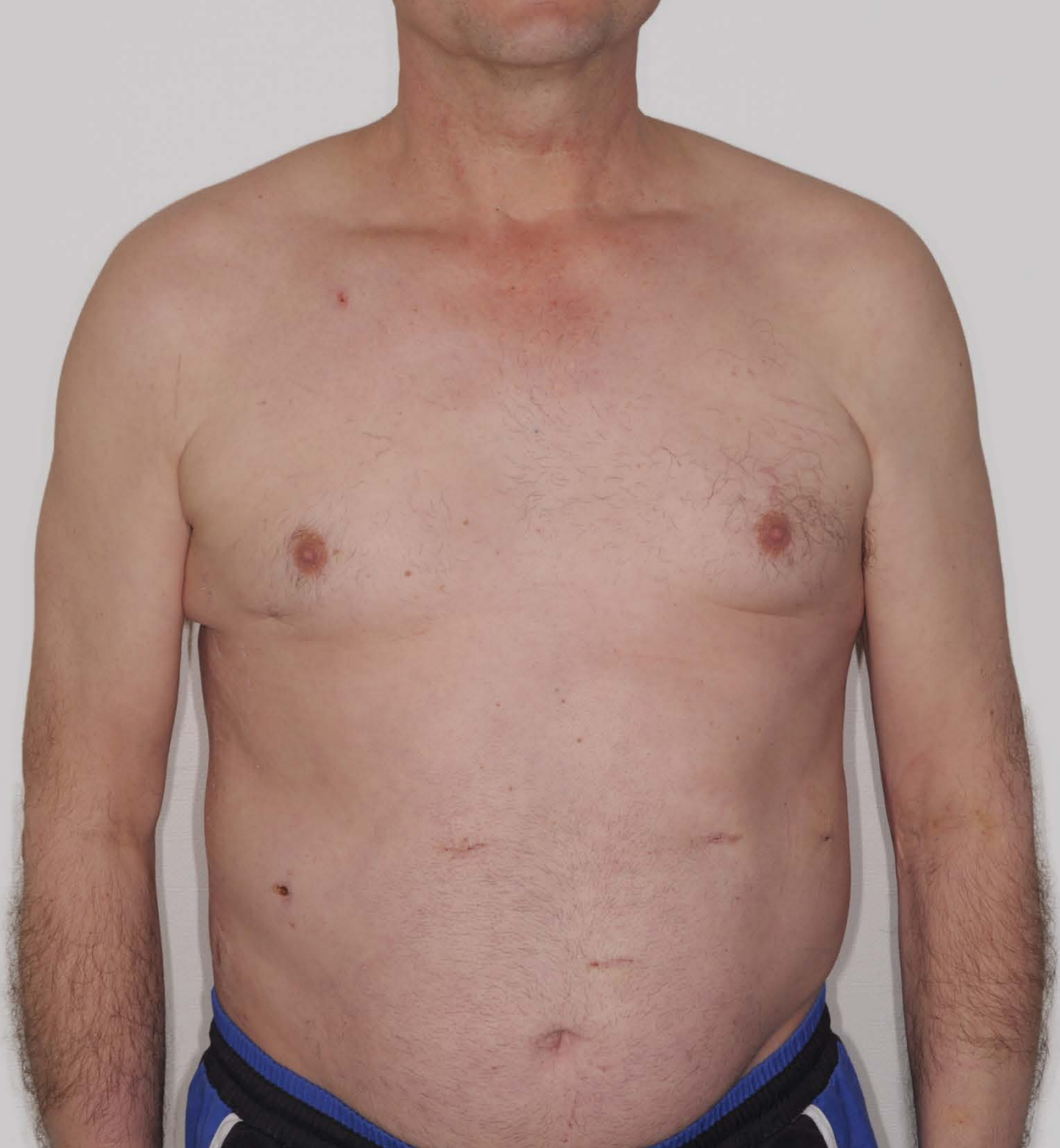
- 19 consecutive patients with preemptive ENP for 4-6 days
- Anastomotic leakage 5% (1/20)
- Median CCI 20.9 (IQR 0-26.2)



Gubler, Vetter, Gutschow *Dis Esophagus* 2018

MIC Ivor Lewis Ösophagektomie









Zusammenfassung

Therapie des Barrett-Karzinoms:

- Interdisziplinäres Management (Endoskopische Resektion, multimodale Therapie, Chirurgie)

Chirurgischer Standard: Transthorakale Ösophagektomie mit 2-Feld LAD

- Intrathorakale Rekonstruktion funktionell überlegen
- Relevante Morbidität, geringe Mortalität
- Therapie in High-volume Zentren

Minimal-invasive Techniken trotz geringer Evidenz etabliert

- Multiple technische Varianten
- Lange Lernkurve beim MIC Vorgehen
- Chirurgischen Komplikationen (Insuffizienz) haben Einfluss auf Langzeitüberleben