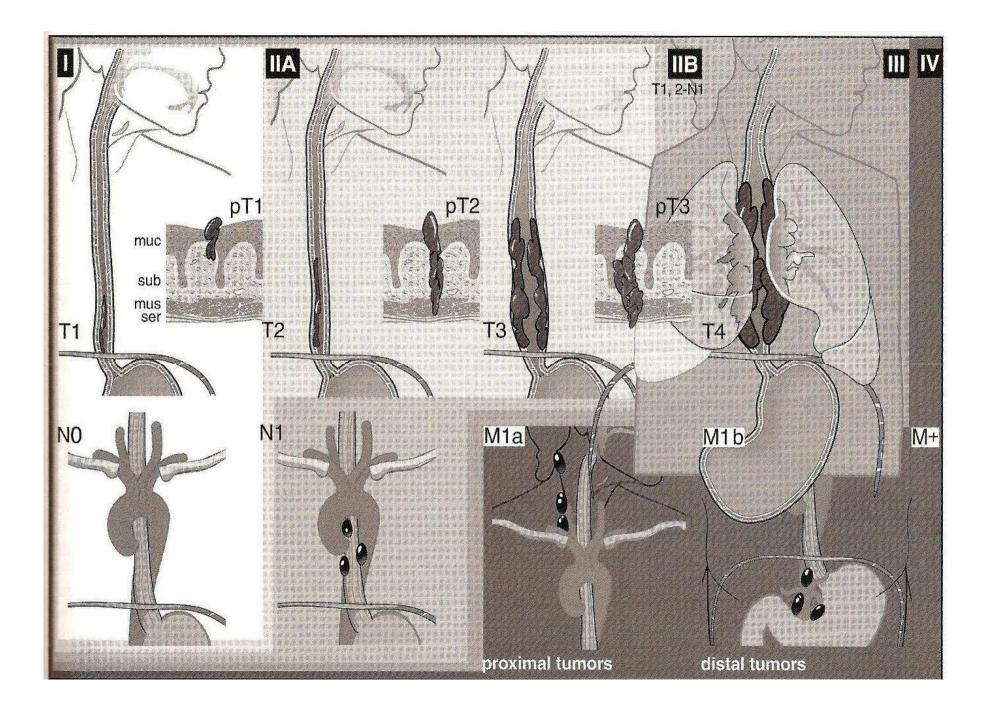
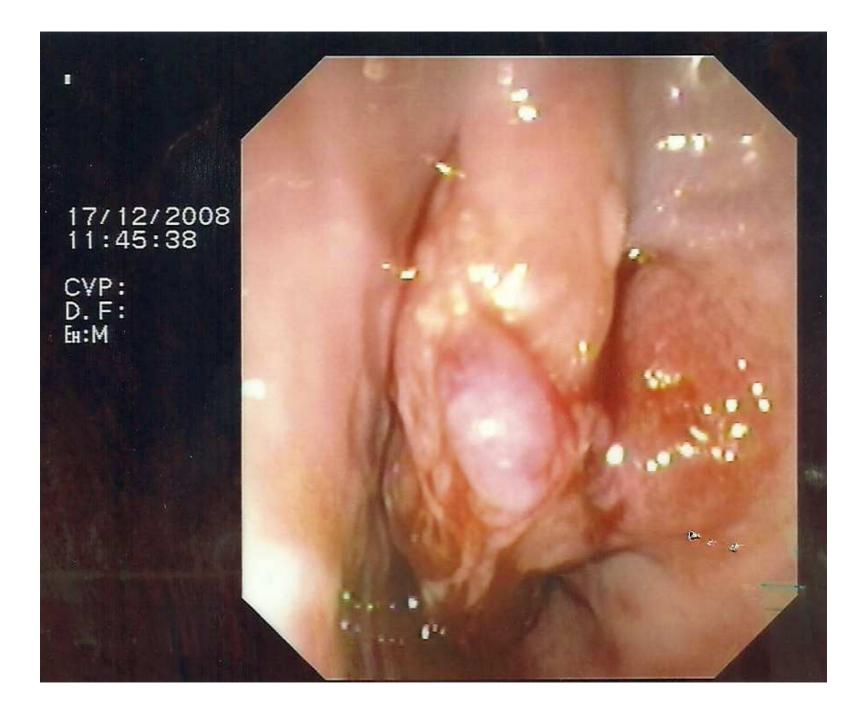
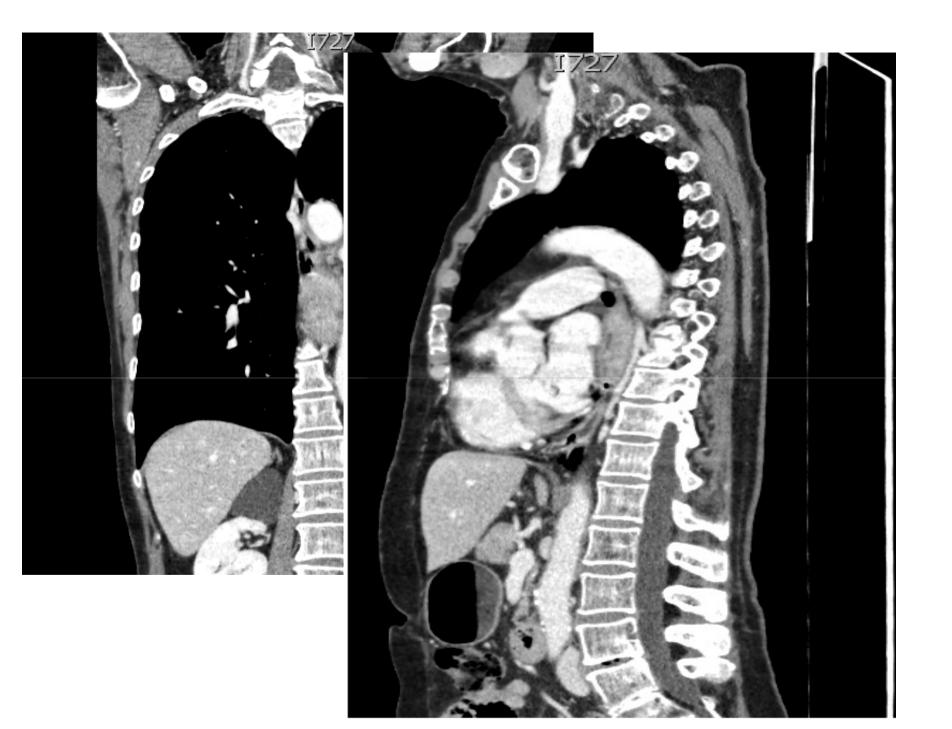
Morbidità e mortalità perioperatoria in pz sottoposti a RT preoperatoria per neoplasie dell'esofago







Variabili correlate alla radioterapia

- Dose: 45-50Gy
- Frazionamento: convenzionale vs non
- Volumi: "involved field"
- Tecnica: 2D vs 3D vs tecniche speciali (IMRT, V-MAT, Tomo ecc)
- Associazione chemioterapia

Variabili correlate al paziente

- Comorbidità:
- Polmonari
- Cardiache
- Metaboliche
- Vascolari
- età; KPS
- Stadio di malattia

Morbidità maggiori

-Sanguinamento

- -Insufficienza respiratoria (ARDS)
- -Deiscenza anastomosi

-Polmonite

- -Versamento pleurico
- -Pneumotorace
- -Versamento pericardico
- -Cardiopatia ischemica

Vantaggi terapia preoperatoria

- Aumento pRC,
- Aumento resezioni RO,
- Aumento controllo locale
- Beneficio OS a 2 anni: 13%



BRIEF ARTICLE

Neoadjuvant chemoradiotherapy for resectable esophageal carcinoma: A meta-analysis

RESULTS: Eleven randomized controlled trials (RCTs) including 1308 patients were selected. Neoadjuvant chemoradiotherapy significantly improved the overall survival compared with surgery alone. Odds ratio (OR) [95% confidence interval (CI), P value], expressed as neoadjuvant chemoradiotherapy and surgery vs surgery alone, was 1.28 (1.01 - 1.64, P = 0.05) for 1-year survival, 1.78 (1.20-2.66, P = 0.004) for 3-year survival, and 1.46 (1.07-1.99, P = 0.02) for 5-year survival. Postoperative mortality increased in patients treated by neoadjuvant chemoradiotherapy (OR: 1.68, 95% CI: 1.03-2.73, P = 0.04), but incidence of postoperative complications was similar in two groups (OR: 1.14, 95% CI: 0.88-1.49, P = 0.32).

Review: Comparison: Outcome:	Neoadjuvant chemoradiotherapy for resectable esophageal carcinoma: A meta-analysis CRT group <i>vs</i> S group Complication after surgery					
Study or		CRT	S	OR (fixed)	Weight	OR (fixed)
sub-category		<i>n/</i> N	<i>n/</i> N	95% CI	%	95% CI
Nygaard <i>et al⁽¹³</i>	^{ij} 1992	16/34	13/38		6.29	1.71 (0.66, 4.42)
Apinop <i>et al</i> ^[14] 1994		8/26	5/34	_	2.90	2.58 (0.73, 9.11)
Le Prise et al ⁽¹⁵⁾ 1994		14/35	18/42	_	9.50	0.89 (0.36, 2.21)
Bosset <i>et al⁽¹⁷⁾ 1</i> 997		45/138	36/137	-+ -	23.56	1.36 (0.81, 2.29)
Urba <i>et al⁽⁹⁾</i> 2001		8/47	7/50	_	5.45	1.26 (0.42, 3.80)
An <i>et al^[12] 2</i> 003		16/48	16/49	_	10.21	1.03 (0.44, 2.40)
Lee <i>et al</i> ⁽⁷⁾ 2004		13/35	19/48		9.75	0.90 (0.37, 2.21)
Burmeister <i>et al⁽¹⁹⁾</i> 2005		63/105	70/110	B	26.46	0.86 (0.49, 1.49)
Natsugoe <i>et al</i> l ⁽¹¹⁾ 2006		7/20	7/23		4.10	1.23 (0.34, 4.42)
Tepper <i>et al</i> l ^{aj} 2008		24/26	24/26		1.79	1.00 (0.13, 7.69)
Total (95% CI)		514	557	•	100.00	1.14 (0.88, 1.49)
Total events: 2:		· /				
		4.43, ďf = 9 (P = 0.	88), <i>I</i> ² = 0%			
Test for overall	effect:Z = 1	.00 (P = 0.32)		, , , , , , , , ,		
			C	.1 0.2 0.5 1 2 5 10)	
				CRT + S S		
Total (95 % CI)		546	589		100.00	1.68 (1.03, 2.73)
Total events	s: 44 (CRT), 3	30 (S)		•		
Test for het	eroaeneitv : h	(² = 5.73, df = 8 (P :	$= 0.68$), $I^2 = 0\%$			
		= 2.09 (P = 0.04)	,			
	aan enect. Z	- 2.09 (- 0.04)				
				0.1 0.2 0.5 1 2 5	10	
				CRT + S S		



Neoadj Treatment-related mortality and morbidity A Revi

Kaklamanos et al. could not find a significant difference in treatment-related mortality between neoadjuvant CRT plus surgery versus surgery alone [8]. The overall rate of postoperative adverse events was not different between the CRT group and the surgery alone group. However, there was a significant effect of CRT on postoperative mortality (90 days) with an odds ration (OR) of 2.1. This increased risk was confirmed in an analysis of observational data including 3,592 patients [34]. Excluding the trials of Bosset et al. [20] resulted in loss of significance [7]. The rate of adverse events was not significantly different between the two treatment arms, but a trend in favor of surgery alone was described for both operative mortality and all treatment mortality.



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BRIEF ARTICLE

Effect of neoadjuvant chemoradiotherapy on prognosis and surgery for esophageal carcinoma

Review: Impact of neoadjuvant chemoradiotherapy on prognosis and surgery for esophageal carcinoma

Co Qu Moreover, the rate of adverse treatment events Sb showed no significant difference between the two groups 19 (OR: 1.33, 95% CI: 0.94-1.88, P = 0.04). However, there 19 19 was a trend in favor of surgery alone for operative mor-19 20 20 tality (OR: 1.78, 95% CI: 1.14-2.78, P = 0.79; Figure 3). 20 20 although there was no significant difference in all treat-20 20 20 ment mortality between CRTS and S groups (OR: 1.12, 20 20 95% CI: 0.89-2.48, P = 0.503). Tol

Test for heterogeneity: $\chi^2 = 6.28$, dF = 10 (P = 0.79), $f^2 = 0\%$ Test for overall effect: Z = 2.53 (P = 0.01)

> 0.1 0.2 0.5 1 2 5 10 Favours CRTS Favours S

Impact of Induction Concurrent Chemoradiotherapy on Pulmonary Function and Postoperative Acute Respiratory Complications in Esophageal Cancer*

Study objective: To evaluate the effects of induction concurrent chemoradiotherapy (cCRT) on pulmonary function and postoperative acute respiratory complications (PARCs).

Design: A retrospective review of our patients treated with induction cCRT to determine the impact on pulmonary function and identify predictors of PARCs. Correlations were sought between patient demographics, clinical characteristics, pre-cCRT and post-cCRT pulmonary function, radiotherapy dose, chemotherapy agents, and the development of PARCs.

Participants: One hundred fifty-five patients treated in three separate clinical trials were identified; 47 patients received 30 Gy (150 cGy bid) of radiation concurrently with a single course of cisplatin/5-fluorouracil (5FU), and 108 patients received 45 Gy (150 cGy bid in a split course) concurrent with two courses of either cisplatin/5FU (n = 69) or cisplatin/paclitaxel (n = 39). Esophagectomy was performed in 141 of these 155 patients following cCRT.

Results: cCRT was only associated with significant worsening of the diffusion capacity of the lung for carbon monoxide (DLCO), which decreased a median of 21.7% in the 45-Gy group (p = 0.007), and 8.6% in the 30-Gy group (p = 0.07). This DLCO decrease was statistically greater in the 45-Gy group than in the 30-Gy group (p = 0.02). PARCs developed in 18 patients. Percentage of predicted FEV₁ and FVC, both before and after cCRT, were both significantly higher in patients without PARCs than in patients with PARCs (p = 0.031 and p = 0.010, respectively). Post-cCRT DLCO was also significantly worse in patients with PARCs (p = 0.002). PARCs occurred significantly more often among those treated with 45 Gy (17 of 102 patients) compared to those treated with 30 Gy (1 of 39 patients) [p = 0.025]. In the 18 patients with PARCs, the median survival was only 2.1 months. This was significantly less than the 16.4-month median survival in the 123 patients who did not have PARCs (p = 0.001).

Conclusions: In patients treated with induction cCRT, higher radiation doses result in increasing impairment of gas exchange. <u>PARCs were more likely in those patients with lower lung volumes</u>, lower post-cCRT DLCO, and in those receiving higher radiation doses. These acute respiratory complications were also associated with a significant reduction in patient survival.

(CHEST 2005; 128:250-255)

Association of Age and Survival in Patients With Gastroesophageal Cancer Undergoing Surgery With or Without Preoperative Therapy

Fadi Braiteh, MD¹; Arlene M. Correa, PhD²; Wayne L. Hofstetter, MD²; David C. Rice, MD²; Ara A. Vaporciyan, MD²; Garrett L. Walsh, MD²; Jack A. Roth, MD²; Reza J. Mehran, MD²; Stephen G. Swisher, MD²; and Jaffer A. Ajani, MD¹

BACKGROUND: Meticulous selection of patients for esophageal cancer surgery is critical, because major surgical intervention can cause considerable consequences. For this study, the authors explored their institution's large surgical experience to examine the impact of age on long-term patient survival and surgical complications. **METHOD**: Six hundred consecutive patients with esophageal cancer who underwent surgery (409 patients received preoperative therapy, and 191 patients underwent surgery first) were analyzed. All demographic information (including American Society of Anesthesiology risk scores) and therapy-related information was collected retrospectively. Multiple statistical methods were used to assess survival rates and surgical complications and their correlation with patient age. Twenty-one patients (30-day mortality) first were excluded (n = 600) and then were included (n = 621) in the analysis. **RESULTS**: By using the median age (<60 years) as the cutoff point and creating 2 subgroups (ages 61 years to 70 years and aged >70 years) in patients older than the median age, univariate analysis demonstrated a higher risk of death with increasing age (P = .019). In multivariate analysis, increasing age was an independent prognosticator of poor overall survival (P = .041). The inclusion of 30-day mortality did not alter the results. Surgical complications were statistically significantly higher in older patients compared with younger patients in the following categories: aspiration pneumonia, adult respiratory distress syndrome, cardiovascular, neurologic, and miscellaneous complications. **CONCLUSIONS**: The data in this study demonstrated that patients aged \leq 60 years who underwent surgery for esophageal cancer achieved the best overall survival and experienced fewer surgical complications than patients aged >70 years. Age was identified as an important variable in the selection of patients for esophageal cancer surgery. Cancer 2009;115:4450-8. © 2009 American Cancer Society.

Int J Radiat Oncol Biol Phys. 2011

Do elderly patients experience increased perioperative or postoperative morbidity or mortality when given neoadjuvant chemoradiation before esophagectomy? Fogh SE, Yu A, Kubicek GJ, Scott W, Mitchell E, Rosato EL, Berger AC.

BACKGROUND: We compared the perioperative morbidity and mortality of patients 70 years old and older with those of patients younger than 70 who received CRT followed by esophagectomy and sought to identify preoperative risk factors that may predict higher risk of postoperative death or complications.

METHODS AND MATERIALS: We identified 260 patients who underwent preoperative chemoradiotherapy followed by esophagectomy. The association of age with postoperative death and complications was evaluated. The Charlson index, prior cardiac history, and diabetes were identified as preoperative risk factors and were evaluated as potential confounders or effect modifiers.

RESULTS: Cardiac disease and the Charlson index were potential modifiers of the effect of age on length of hospital stay (p = 0.08 and p = 0.07, respectively) and postoperative complications (p = 0.1 and p = 0.2) but were not statistically significant. There was a slight non significant decrease in the risk of death in elderly patients after adjustment for the Charlson index (p = 0.2).

CONCLUSION: No significant differences were detected with respect to morbidity and mortality in elderly patients. The presence of cardiac disease, higher scores on the Charlson index, or diabetes did not significantly influence length of stay, postoperative complications, or postoperative death. Given the potential to improve outcomes, this regimen should not be discounted in elderly patients.

Int J Radiat Oncol Biol Phys. 2010

neoadjuvant RCT followed by surgery (RCTS).

Influence of irradiated lung volumes on perioperative morbidity and mortality in patients after neoadjuvant radiochemotherapy for esophageal cancer. Dähn D, Martell J, Vorwerk H, Hess CF, Becker H, Jung K, Hilgers R, Wolff HA, Hermann RM, Christiansen H. PURPOSE: Increased perioperative pulmonary toxicity in terms of acute respiratory distress syndrome (ARDS) has been linked to radiation exposure of the lungs. In our study we evaluated perioperative morbidity and mortality in patients with cancer Stages IIA-IVA treated with curative intent either with surgery alone (S) or with

PATIENTS AND METHODS: Between 1996 and 2003, 55 patients received S, and 98 received RCTS. In the RCTS group, most patients received two cycles of 5-fluorouracil plus cisplatinum simultaneously with normofractionated radiotherapy (40Gy). Four weeks later they underwent surgery. Endpoints were the incidence of acute lung injury (ALI), ARDS, other postoperative complications, and mortality within 31 days.

RESULTS: Between both groups there were no significant differences between the incidence and severity of ALI and ARDS (RCTS: 42.9%, 42.9%; S: 45.5%, 38.2%). Furthermore, there were no significant differences in the incidences of pneumonia, pleural effusion, and pneumothorax (RCTS 29.6% vs. S 16.4%, p = 0.07). Perioperative complication rates and mortality did not vary significantly (mortality after RCTS 5.1% vs. S 3.6%). A detailed analysis of 54 RCTS patients according to lung dose-volume histograms did not show any correlation between ARDS and pulmonary exposure. In univariate analysis, only respiratory comorbidity correlated with ARDS.

CONCLUSION: Neoadjuvant cisplatinum and 5-fluorouracil-based RCT apparently has no detrimental impact on the postoperative course.

Eur J Cardiothorac Surg. 2008 Airway colonisation and postoperative pulmonary complications after neoadjuvant therapy for oesophageal cancer.

D'Journo XB, Michelet P, Papazian L, Reynaud-Gaubert M, Doddoli C, Giudicelli R, Fuentes PA, Thomas PA.

OBJECTIVE: To evaluate the clinical relevance of preoperative airway colonization in patients undergoing oesophagectomy for cancer after a neoadjuvant chemoradiotherapy. METHODS: From 1998 to 2005, 117 patients received neoadjuvant chemoradiotherapy for advanced stage oesophageal cancer. Among them, 45 non-randomised patients underwent a bronchoscopic bronchoalveolar lavage (BAL group) prior to surgery to assess airways colonisation. The remaining patients (n=72) constituted the control group.

RESULTS: Thirteen of the 45 BAL patients (28%) had a preoperative bronchial colonisation by either potentially pathogenic micro-organisms (PPMs) (n=7, 16%) or non-potentially pathogenic micro-organisms (n=6, 13%). Cytomegalovirus (CMV) was cultured from BAL in four patients. Pre-emptive therapy was administrated in seven patients: four antiviral and three antibiotic prophylaxes. Postoperatively,14 patients (19%) developed acute respiratory distress syndrome (ARDS) in the control group and three (7%) in the BAL group (p=0.064). The cause of ARDS was attributed to CMV pneumonia in six control group patients on the basis of the results of open lung biopsies (n=3) or BAL cultures (n=3) versus none of the BAL group patients (p=0.08). Timing for extubation was shorter in the BAL group (mean 13+/-3 h) as compared with the control group (mean 19.5+/-14 h; p=0.039).

In-hospital mortality was not significantly lower in BAL group patients when compared to that of control group patients (8% vs 12.5%).

CONCLUSIONS: Airway colonisation by PPMs after neoadjuvant therapy is suggested as a possible cause of postoperative ARDS after oesophagectomy. Pre-emptive treatment of bacterial and viral (CMV) colonisation seems an effective option to prevent postoperative pneumonia.

Br J Surg. 2006 Impact of preoperative radiochemotherapy on postoperative course and survival in patients with locally advanced squamous cell oesophageal carcinoma. Mariette C, Piessen G, Lamblin A, Mirabel X, Adenis A, Triboulet JP.

BACKGROUND: The aim of this study was to determine the effect of neoadjuvant radiochemotherapy (RCT) on postoperative complications and survival after surgery for locally advanced oesophageal squamous cell carcinoma.

METHODS: Postoperative course and survival were compared in 144 patients who had neoadjuvant RCT and 80 control patients who had surgery alone for locally advanced oesophageal squamous cell carcinoma (radiological stage T3, N0 or N1, M0).

RESULTS: The two groups were comparable in terms of American Society of Anesthesiologists grade, age, sex, weight loss, tumour location, presence of lymph node metastasis and surgical approach. Postoperative mortality rates were 6.3 and 9 per cent (P=0.481), with morbidity rates of 40.3 and 41 percent (P=0.887) in the RCT and control group respectively. Complete resection (R0) rates were 74.3 and 48 percent respectively (P<0.001). Significant downstaging was observed in the RCT group (P<0.001), with 16.0 percent of patients having a complete pathological response. Median survival was 29 versus 15 months, and the 5-year survival rate 37 versus 17 percent (P=0.002) in RCT and control groups respectively.

CONCLUSION: Neoadjuvant RCT significantly enhanced R0 resection and survival rates in patients with stage T3 oesophageal squamous cell carcinoma, with no increase in postoperative mortality and morbidity rates.

Ann Thorac Surg. 2011

Morbidity and mortality after esophagectomy following neoadjuvant chemoradiation. Merritt RE, Whyte RI, D'Arcy NT, Hoang CD, Shrager JB.

BACKGROUND: Neoadjuvant chemoradiation (CRT) is an accepted treatment for locally advanced esophageal carcinoma. A survival benefit has not been definitively established, and there is concern that chemoradiation may increase postoperative morbidity and mortality.

METHODS: A retrospective review was made of 138 patients treated for esophageal carcinoma between January 1999 and December 2009. Fifty-four patients who underwent CRT followed by esophagectomy were compared with 84 patients who underwent esophagectomy alone.

RESULTS: The chemoradiation and esophagectomy alone cohorts were well matched on all preoperative variables. There was a higher percentage of Ivor Lewis procedures in the esophagectomy alone cohort (82.0%) compared with the CRT cohort (59.3%; p = 0.006). Thirty-five percent of the CRT group underwent transhiatal esophagectomy. Thirty-day mortality was 6.0% (5 of 84) in the esophagectomy alone cohort compared with 1.9% (1 of 54) in the CRT cohort (p = 0.5). Similarly, mean intensive care unit stay (4.7 versus 6.5 days; p = 0.5), ventilator time (2.4 versus 4.2 days; p = 0.5), and length of stay (13.5 versus 17 days; p = 0.2) did not differ significantly between the groups. The overall major complication rates were similar in the CRT and esophagectomy alone cohorts: 57.4% versus 56% (p = 0.98). Multivariate analysis determined that coronary artery disease (p = 0.01;odds ratio 3.5) and transthoracic esophagectomy (p = 0.05; odds ratio 1.4) were predictive of development of postoperative complications. Only cervical anastomotic location (p =0.04; odds ratio 3.0) was predictive of anastomotic leak on multivariate analysis.

CONCLUSIONS: Neoadjuvant chemoradiation does not appear to increase postoperative morbidity or mortality after esophagectomy. Major postoperative complications are associated with the transthoracic approach and preoperative coronary artery disease. Int J Cardiovasc Imaging. 2009

The clinical implications of myocardial perfusion abnormalities in patients with esophageal or lung cancer after chemoradiation therapy.

Gayed I, Gohar S, Liao Z, McAleer M, Bassett R, Yusuf SW.

PURPOSE: This study aims to identify the clinical implications of myocardial perfusion defects after chemoradiation therapy (CRT) in patients with esophageal and lung cancer.

METHODS: We retrospectively compared myocardial perfusion imaging (MPI) results before and after CRT in 16 patients with esophageal cancer and 24 patients with lung cancer.

RESULTS: Eleven females and twenty nine males at a mean age of 66.7 years were included. Five patients (31%) with esophageal cancer and seven patients (29%) with lung cancer developed myocardial ischemia in the RT field at mean intervals of 7.0 and 8.4 months after RT. The patients were followed-up for mean intervals of 15 and 23 months in the esophageal and lung cancer groups, respectively. Seven patients in each of the esophageal (44%) and lung (29%) cancer patients (P = 0.5) developed cardiac complications of which one patient with esophageal cancer died of complete heart block. Six out of the fourteen patients (43%) with cardiac complication had new ischemia on MPI after CRT of which only one developed angina. The remaining eight patients with cardiac complications had normal MPI results. MPI result was not a statistically significant predictor of future cardiac complications after CRT. A history of congestive heart failure (CHF) (P =0.003) or arrhythmia (P = 0.003) is a significant predictor of cardiac morbidity after CRT in univariate analysis but marginal predictors when multivariate analysis was performed (P = 0.06 and 0.06 for CHF and arrhythmia, respectively).

CONCLUSIONS: Cardiac complications after CRT are more common in esophageal than lung cancer patients but the difference is not statistically significant. MPI abnormalities are frequently seen after CRT but are not predictive of future cardiac complications. A history of arrhythmia or CHF is significantly associated with cardiac complications after CRT. J Surg Res. 2009

Correlations between neoadjuvant treatment, anemia, and perioperative complications in patients undergoing esophagectomy for cancer.

Melis M, McLoughlin JM, Dean EM, Siegel EM, Weber JM, Shah N, Kelley ST, Karl RC. INTRODUCTION: The influence of preoperative hemoglobin levels on outcomes of patients undergoing esophagectomy for cancer is not clearly defined. METHODS: From a retrospective esophageal database, 413 patients were identified. The independent association of anemia, blood transfusion, and combined modality treatment on risk of postoperative complications were examined using multiple logistic regression.

RESULTS: Overall 197 (47.6%) patients were

preoperatively found to be anemic, and those who had received combined modality treatment were more likely to be anemic (60.6% versus 30.7%, P < 0.001). Anemic patients required more blood transfusions than non anemic patients (46.7% versus 29.6%, P < 0.001). Seventy-five percent of patients who required transfusion during the hospital stay had received combined modality treatment (P = 0.01). Combined modality treatment and anemia were not associated with increased risk of complications. Patients with any perioperative complication and surgical site infections were more likely to have received blood transfusion compared to patients without complications (OR = 1.73; 95% CI 1.04-2.87 and OR = 2.98; 95% CI 1.04-8.55; respectively).

CONCLUSIONS: Overall, we determined that administration of neoadjuvant treatment to esophageal cancer patients was not associated with an increased rate of perioperative complications. Preoperative anemia did not predict worsened short-term outcomes, but increased the chances of red blood cell transfusion, which were significantly associated with higher overall complications and increased risk of surgical site infections. These data confirm previous studies that allogenic red blood cell transfusions are independent risk factors for increased morbidity and mortality and should be minimized during surgery for esophageal cancer.

J Thorac Oncol. 2009 Induction chemoradiotherapy increases pleural and pericardial complications after esophagectomy for cancer. Murthy SC, Rozas MS, Adelstein DJ, Mason DP, Calhoun R, Rybicki LA, Feng J, Blackstone EH, Rice TW.

METHODS: Between March 1987 and November 2001, 291 patients with clinical stage > or = IIA esophageal cancer underwent esophagectomy; 106 received induction chemoradiotherapy. A propensity score incorporating clinical stage and histopathology was used to identify 100 matched pairs of induction chemoradiotherapy and surgery-only patients. Among these, occurrence of pleural effusion, pericardial effusion, and pericarditis was ascertained by follow-up. Time-related occurrence, risk factors, and association with survival were assessed by repeated-events analyses.

RESULTS: During follow-up, 61 induction chemoradiotherapy patients experienced at least one pleural or pericardial complication, as did 46 propensity-matched surgery-only patients. Most occurred within 1 year, with 1-year freedom from occurrence only 34% after induction chemoradiotherapy and 59% after surgery only (p = 0.02). Risk of pleural effusion was nearly twice as great (hazard ratio 1.7,p =0.0004) and pericardial complications 5 times greater (hazard ratio 5.3, p = 0.0005) after induction chemoradiotherapy than after surgery alone. Complications after induction chemoradiotherapy required intervention somewhat more frequently (58% versus 47%, p = 0.18), although they did not diminish subsequent survival (p > 0.8). CONCLUSIONS: Benign pleural and pericardial complications occur surprisingly frequently after esophagectomy, particularly when induction chemoradiotherapy is employed. This must be factored into discussions of morbidity for multimodality treatment strategies for locally advanced esophageal cancer and should be considered distinct from acute toxicity of induction chemoradiotherapy reported.

Ann Thorac Surg. 2012

Does the timing of esophagectomy after chemoradiation affect outcome? Kim JY, Correa AM, Vaporciyan AA, Roth JA, Mehran RJ, Walsh GL, Rice DC, Ajani JA, Maru DM, Bhutani MS, Welsh J, Marom EM, Swisher SG, Hofstetter WL. BACKGROUND: After neoadjuvant chemoradiation (CXRT) for esophageal cancer, surgery has traditionally been recommended to be performed within 8 weeks. However, surgery is often delayed for various reasons. The optimal timing of esophagectomy after CXRT is unknown.

METHODS: From a prospective database, we analyzed 266 patients with resected esophageal cancer who were treated with neoadjuvant CXRT from 2002 to 2008. Salvage resections were excluded from this analysis. We compared patients who had surgery within 8 weeks of CXRT and those who had surgery after 8 weeks. We used multivariable analysis to determine whether increased interval between chemoradiation and surgery was independently associated with perioperative complication, pathologic response, or overall survival.

RESULTS: One hundred fifty patients were resected within 8 weeks and 116 were resected greater than 8 weeks after completing CXRT. Mean length of operation, intraoperative blood loss, anastomotic leak rate, and perioperative complication rate were similar for the two groups. Pathologic complete response rate and overall survival were also similar for the two groups (p=not significant). In multivariable analysis, timing of surgery was not an independent predictor of perioperative complication, pathologic complete response, or overall survival.

CONCLUSIONS: The timing of esophagectomy after neoadjuvant CXRT is not associated with perioperative complication, pathologic response, or overall survival. It may be reasonable to delay esophagectomy beyond 8 weeks for patients who have not yet recovered from chemoradiation. World J Surg. 2010

Factors influencing the long-term survival in patients with esophageal cancer who underwent esophagectomy after chemoradiotherapy. Takeuchi H, Saikawa Y, Oyama T, Ozawa S, Suda K, Wada N, Takahashi T, Nakamura R,Shigematsu N, Ando N, Kitajima M, Kitagawa Y.

BACKGROUND: salvage esophagectomy is a highly invasive procedure with various postoperative complications compared to planned esophagectomy after neoadjuvant chemoradiotherapy (CRT).

METHODS: For the present study we reviewed the surgical procedures, postoperative complications, and the prognosis of 65 consecutive patients with thoracic ESCC who underwent esophagectomy after neoadjuvant (neoadjuvant group: n = 40) or definitive (salvage group: n = 25) CRT.

RESULTS: Most patients underwent right-transthoracic extended esophagectomy and reconstruction using gastric conduit by way of subcutaneous route with left cervical anastomosis. The incidence of postoperative pneumonia was found to be higher in the salvage group than in the neoadjuvant group. In both groups, the survival of patients with R0 resection was significantly better than those with R1/R2 resection. Moreover, in the salvage group, the postoperative survival rate of patients with pneumonia or bacteremia/sepsis was significantly lower than that for patients who did not suffer the same complications. In the neoadjuvant group,R0 resection was selected to be the only independent prognostic factor in univariate and multivariate analysis. In contrast, in the salvage group, R0 resection and bacteremia/sepsis remained significant and were independent of the other factors in multivariate analysis.

CONCLUSIONS: This study reveals that postoperative morbidity affects not only the perioperative mortality but also the long-term survival of patients with ESCC who undergo salvage esophagectomy after definitive CRT.

J Surg Oncol.2009 Salvage esophagectomy after definitive chemoradiotherapy for thoracic esophageal cancer. Miyata H, Yamasaki M, Takiguchi S, Nakajima K, Fujiwara Y, Nishida T, Mori M, Doki Y.

BACKGROUND AND OBJECTIVES: the role of salvage esophagectomy has not been fully evaluated. The aim of this study was to compare the outcome of salvage esophagectomy after high-dose definitive CRT with neoadjuvant CRT.

METHODS: From 1994 to 2007, 33 patients with thoracic esophageal cancer underwent salvage esophagectomy after definitive CRT, and 115 patients underwent neoadjuvant CRT followed by surgery.

RESULTS: The postoperative mortality rate in the salvage group (12%) was higher than in the neoadjuvant group (3.6%, P = 0.059). The rates of postoperative complications were significantly higher in the salvage group than in neoadjuvant group: Anastomotic leakage (39% vs. 22%, respectively, P = 0.049), bleeding (15% vs. 1.7%, respectively, P = 0.002), cardiovascular complications (24% vs. 5.4%, respectively, P = 0.001). Univariate analysis showed that pretherapy T stage, pretherapy lymph node status, pathological T stage, and operative curability were significant prognostic factors affecting survival of patients who underwent salvage esophagectomy. In particular, patients with cT3-T4 tumors or cN1 tumors before definitive CRT showed worse prognosis after salvage esophagectomy.

CONCLUSIONS: Salvage esophagectomy after high-dose definitive CRT was associated with higher postoperative mortality and morbidity rates compared with neoadjuvant CRT. Only selected patients can be rescued by salvage esophagectomy.

J Thorac Cardiovasc Surg. 2009 Predictors of major morbidity and mortality after esophagectomy for esophageal cancer: a Society of Thoracic Surgeons General Thoracic Surgery Database risk

adjustment model. Wright CD, Kucharczuk JC, O'Brien SM, Grab JD, Allen MS; Society of Thoracic Surgeons General Thoracic Surgery Database.

METHODS: The Society of Thoracic Surgeons General Thoracic Database was queried for all patients treated with esophagectomy for esophageal cancer between January 2002 and December 2007.

RESULTS: There were 2315 esophagectomies performed by 73 participating centers. Hospital mortality was 63/2315 (2.7%). Major morbidity (defined as reoperation for bleeding [n = 12], anastomotic leak [n = 261], pneumonia [n = 188], reintubation [n = 227], ventilation beyond 48 hours [n = 71], or death [n = 63]) occurred in 553 patients (24%). Preoperative spirometry was obtained in 923/2315 (40%) of patients. A forced expiratory volume in 1 second < 60% of predicted was associated with major morbidity (P = .0044). Important predictors of major morbidity are: age 75 versus 55 (P = .005), black race (P = .08), congestive heart failure (P = .015), coronary artery disease (P = .017), peripheral vascular disease (P = .009), hypertension (P = .029), insulin-dependent diabetes (P = .009), American Society of Anesthesiology rating (P = .001), smoking status (P = .022), and steroid use (P = .026). A strong volume performance relationship was not observed for the composite measure of morbidity and mortality in this patient cohort.

CONCLUSIONS: Thoracic surgeons participating in the Society of Thoracic Surgeons General Thoracic Database perform esophagectomy with a low mortality. We identified important predictors of major morbidity and mortality after esophagectomy for esophageal cancer. Volume alone is an inadequate proxy for quality assessment after esophagectomy.

Morbidità-mortalità perioperatoria

- DLCO
- "timing" chirurgia dopo terapia preoperatoria
- Colonizzazione tracheo-bronchiale
- Anemia
- Età ???

Morbidità-mortalità perioperatoria

- Benefici potenziali terapia trimodale in termini di controllo locale e sopravvivenza globale
- Importanza selezione paziente
- Non differenze statisticamente significative in termini di tossicità tra terapia preoperatoria + chirurgia vs chirurgia da sola
- Attenzione chirurgia di salvataggio