

Meta-Analysis of Survival After Pleurectomy Decortication Versus Extrapleural Pneumonectomy in Mesothelioma

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Background. This comprehensive meta-analysis was conducted to answer the question as to which procedure, pleurectomy decortication (P/D) or extrapleural pneumonectomy (EPP) is more beneficial to malignant pleural mesothelioma patients' outcome.

Methods. Original research studies that evaluated long-term outcomes of P/D versus EPP were identified, from January 1990 to January 2014. The combined percent perioperative and 2-year mortality, and median survival were calculated according to both a fixed and a random effect model. The Q statistics and I^2 statistic were used to test for heterogeneity between the studies.

Results. There were 24 distinct data sets, for a total of 1,512 patients treated with P/D, and 1,391 treated with EPP. There

was a significantly higher proportion of short-term deaths in the EPP group versus the P/D group (percent mortality meta estimate; 4.5% vs 1.7%; $p < 0.05$). There was no statistically significant difference in 2-year mortality between the 2 groups, but there was significant heterogeneity.

Conclusions. The reanalysis of the large number of studies comparing P/D to EPP suggests that P/D is associated with a 2 $\frac{1}{2}$ -fold lower short-term mortality (peri-operatively and within 30 days) than EPP. Pleurectomy decortication should therefore be preferred when technically feasible.

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Giriş-1

- Malign mezotelyoma, ana etyolojik faktör olan asbest yasaklanmış olmasına karşın giderek daha sık görülmektedir.
- Tedavide kemoterapi, radyoterapi ve cerrahi seçenekleri yer almaktadır.
- Cerrahi tedavi olarak ise ektraplevral pnömonektomi (EPP) (plöroplevral pnömonektomi) ve plörektomi dekortikasyon ameliyatları yapılmaktadır.

Giriş-2

- Hangi cerrahinin daha iyi olduğuna dair, genellikle tek merkezli çalışmalar bulunmaktadır.
- İngiltere’de yapılan ve yayınlanan MARS çalışması EPP’nin sağ kalıma bir yarar sağlamadığını gösterdi.
- Şu ana kadar yapılan 1 metaanaliz ise, 2 cerrahi işlemi karşılaştırarak plörektomi/dekortikasyonun daha yararlı olduğunu işaret etti.

Gereç ve Yöntemler

- Pubmed ve Embase'den 'pleurectomy', 'pneumonectomy', 'malignant pleural mesothelioma' anahtar kelimeleri ile 1990 ile 2014 arasında elde edilen çalışmalar irdelendi: 98 çalışma.
- Her çalışmadan mortalite ve sağkalım verileri alındı.
- I² testi: Heterojenite için kullanıldı.
- Sağkalım verisi: 17 çalışma.
- Kısa dönem komplikasyonlar: 14/24 çalışma.

Table 1. Studies Included in the Meta Analysis

Author, Year	Study Design	Country	Sex M/F	Age (Years), Range, Mean \pm SD	Histology	Stage	Number of Patients Pleurectomy Decortication (P/D) n = 1,512	Number of Patients Extrapleural Pneumonectomy (EPP) n = 1,391
Branscheid D, 1991	Retro (1978-89)	Germany	235/66	22-87, mdn = 59	Epithelial (50%); mixed (25%); sarcomatous (12%); unclassified (13%)	I (2%); II (11%); III (56%); V (15%)	82	76
Allen KB, 1994	Retro (1958-93)	USA	79/17	$\mu = 55.2 \pm 1.5$ (EPP); 63.5 ± 9.6 (P)	Epithelial (56%), mixed (29%), sarcomatous (15%)	I (51%); II (38%); III (8%); IV (3%)	56	40
Pass HI, Krandt K, 1997; Pass HI, Temeck BK, 1997	Reanalysis of clinical trial (1990-95)	USA	78/17	30-77	Epithelial, 60; sarcomatoid, 6, biphasic, 12		39	39
Moskal TL, 1998	Retro (1991-96)	USA	31/9	21-77; $\mu = 60$;	Epithelial (62.5%); biphasic (25%); sarcomatous (12.5%)	I, I I = 13; III, IV = 24	28	7
Lampl L, 1999	Retro (1986-98)	Germany	45/8	n/a	sarcomatous	II & III (P/D)	23	22
Rusch VW, 1999 ^a	Retro (1983-98)	USA	192/39	24-80; mdn = 62	Epithelial = 164 (71%), fibrosarcomatous = 14 (6%). Mixed = 51 (22%), desmoplastic = 1, unk = 1	I = 21; II = 40; III = 102; IV = 68	59	115
Aziz T, 2002	Retro (1989-99)	UK	244/61	34-77; mdn = 57	Epithelial & sarcomatous	I, II, III	47	64
Yom SS, 2003	Phase I trial on PDT	UK	8/1	39-75	Epithelioid = 7, biphasic = 2		8	1
de Vries WJ, 2003	Retro (1976-2001)	South Africa	33/13	35-80	Epithelial, sarcomatoid, mixed	I, II, III	29	17
Rosenzweig KE, 2005	Phase II trial (1994-96)	USA				T2 - T3, N0-N2	6	7
Flores RM, 2007 ^a	Retro (1990-2005)	USA	755/190	26-93,mdn = 66	Epithelioid = 319 (34%), mixed = 99 (10%), sarcomatoid = 44 (5%), unclassified = 483 (51%)	I (2%); II (95); III (24%); IV (16%), unk (48%)	176	208
Okada M, 2008	Retro (1986-2006)	Japan	58/7	35-78; mdn = 60 yrs	Epithelial (74%), mixed (17%), sarcomatous (9%)	I (12%), II (20%), III (62%), IV (6%)	34	31
Schipper PH, 2008	Retro (1985-2003)	USA	236/49	26-91, mdn = 66	Epithelial = 134, nonepithelial = 108, unclassified = 43	IA = 20, IB = 82, II = 24, III = 75, IV = 60, unknown = 24	44	73

(Continued)

Table 1. Continued

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Borasio P, 2008	Retro (1989-2003)	Italy	270/124	28-93; median = 64	Epithelial = 246 (67.2%), biphasic = 84 (23%), sarcomatous = 36 (9.8%), indeterminate = 28		12	15
Yan TD, 2009	Retro (1984-2007)	Australia	390/66	66 \pm 10	Epithelial = 185 (40%), sarcomatoid/biphasic = 183 (40%), unknown = 88 (19%)		250	59
Mineo TC, 2010	Retro (1987-2007)	Italy	63/14	27-82; 61.3 \pm 10	Epithelioid = 50, biphasic = 17, sarcomatoid = 10	I = 21, II = 36, III = 20	44 (10 subtotal)	27
Luckraz H, 2010	Retro (1980-2010)	UK	180/28	58.9 \pm 9.8	Epithelial	I, II, III	90	49
Friedberg JS, 2011	Retro (2004-08)	USA	19/9	27-81	Epithelioid n = 17, sarcomatoid = 2, biphasic = 3	III, IV (85.7 %)	14	14
Rena O, 2012	Retro (1998-2009)	Italy	24/35	56 \pm 11 (EPP); 58.5 \pm 9.5 (P/D)	Epithelial = 29	I, II	37	40
Nakas A, Waller D, 2012; Nakas A, Meyenfeldt E, 2012; [Martin-Ucar AE, 2007]	Retro	UK	181/31	14-72; median = 59	Epithelioid = 160, biphasic = 52		85	127
Lang-Lazdunski L, 2012	Retro (2004-2011)	UK	x	x	Epithelioid & nonepithelioid	I- IV	61	25
Lindenmann J, 2012	Retro (2000-2009)	Austria	47/14	34-82; mean = 63.7	Epithelioid = 48 (78.7%), sarcomatoid = 3 (4.9%), biphasic = 10 (16%)		41	3
Bedirhan MA, 2013	Retro (2001-13)	Turkey	58/18	30-76 (mean 53.2)	Epithelioid = 60		45	31
Bovolato P, 2014	Retro (1982-2012)	Italy	374/129	62.5 (P/D); 58.7 (EPP)	Epithelial 81%	I: 9.5%; II: 27.6%; \geq III: 19%; unk: 43.7%	202	301

^a Partial overlapping of the data sets.

IORT= intraoperative radiation therapy; mdn = median; PDT = photodynamic therapy; unk = unknown.

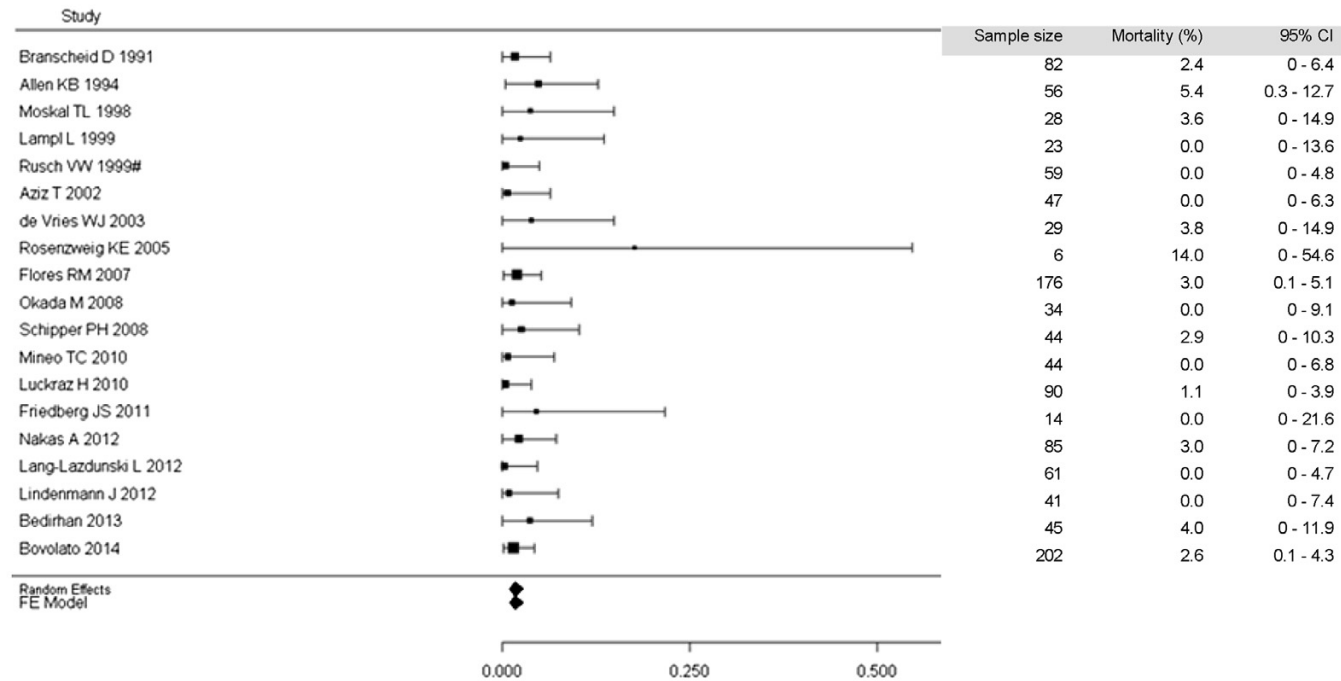
Table 1. Continued

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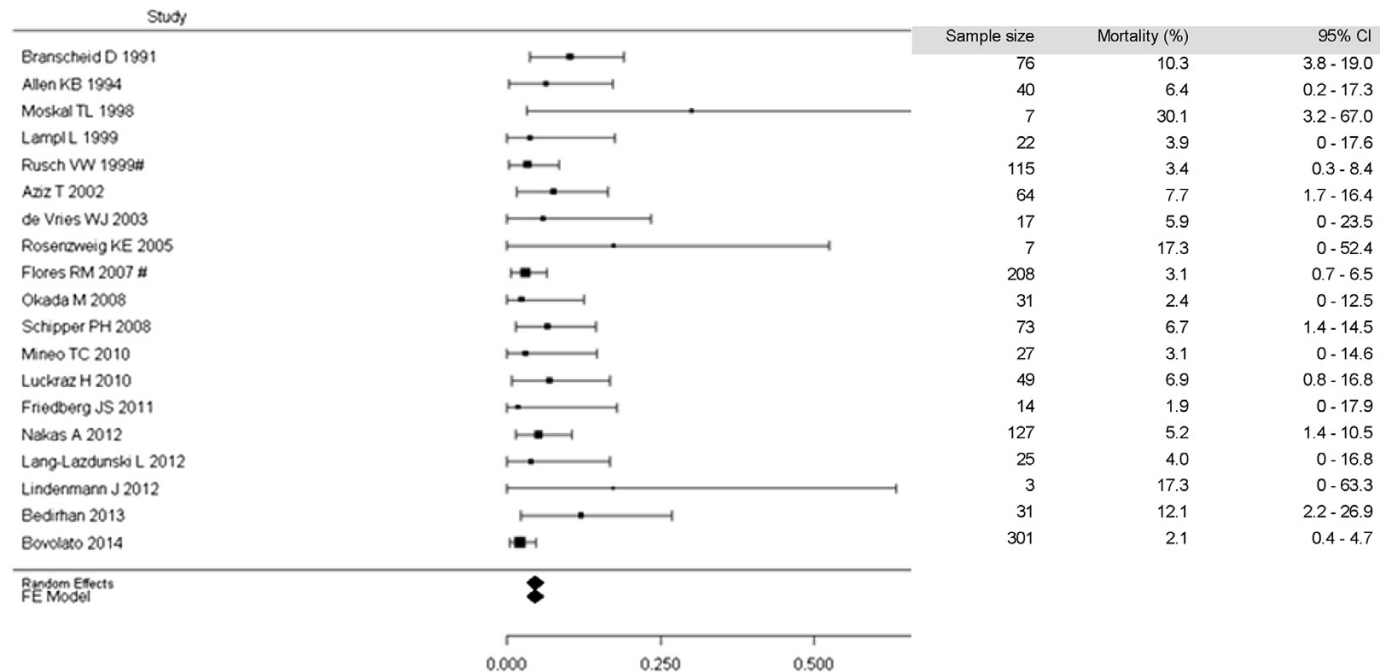
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Pleurectomy/Decortication



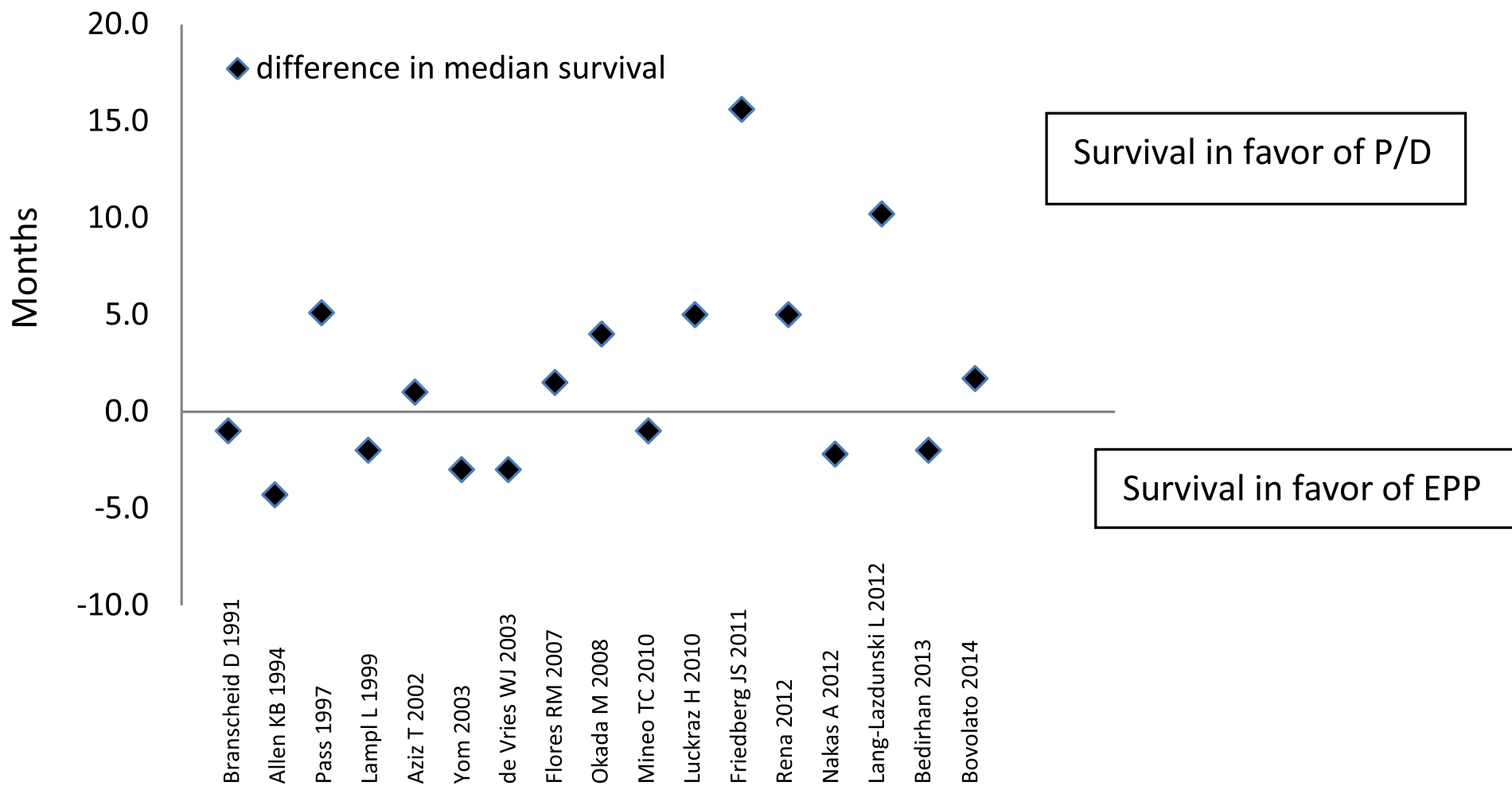
Extrapleural Pneumonectomy



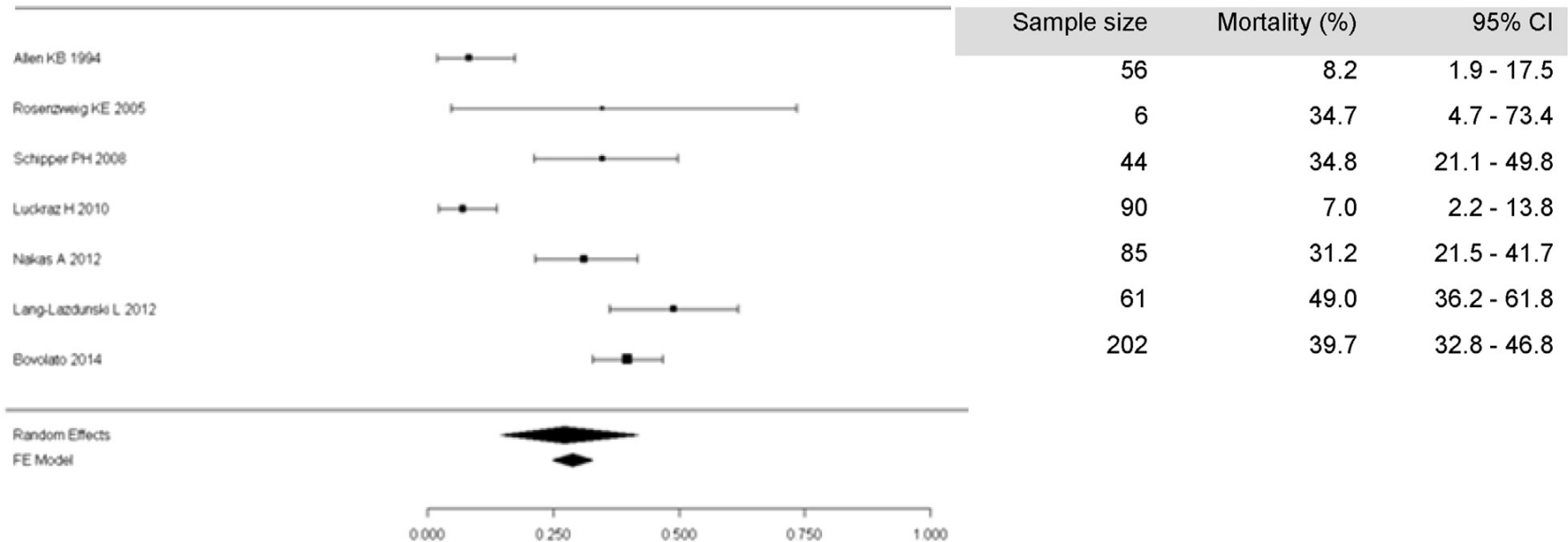
	Pleurectomy/Decortication		Extrapleural Pneumonectomy		P value [^]
	Sample size	Meta % mortality (95% CI)	Sample size	Meta % mortality (95% CI)	
Total (fixed effects)	1166	1.7 (0.9- 2.8)	1237	4.5 (3.2- 6.0)	<0.05
Total (random effects)	1166	1.7 (0.9- 2.8)	1237	4.5 (3.2- 6.0)	<0.05
Q (DF)	7.6 (18)		16.8 (18)		
Significance level	P = 1.0		P=0.53		
I ²	0.0		0.0		

[^] p value tests the statistical difference between percent mortality

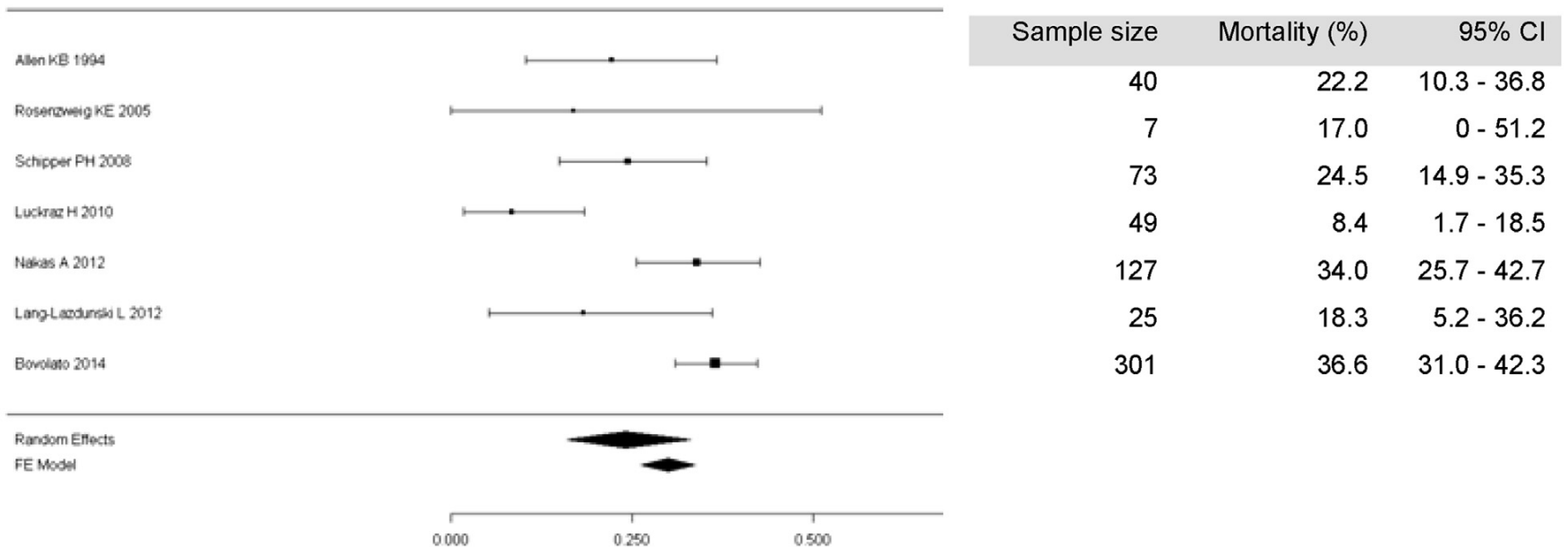
Fig 1. Meta-analysis of short-term mortality (perioperative and 30 days after surgery).



Pleurectomy/Decortication



Extrapleural pneumonectomy



Sağkalım

		Pleurectomy/Decortication		Extrapleural Pneumonectomy	P value
	Sample size	Meta % survival (95% CI)	Sample size	Meta % survival (95% CI)	
Total (fixed effects)	544	28.8 (25.0-32.9)	622	30.0 (26.3-33.8)	0.7
Total (random effects)	544	27.3 (14.7-41.9)	622	24.2 (16.1-33.1)	0.2
Q (DF)	64.3 (6)			25.2 (6)	
Significance level	P<0.0001			P = 0.003	
I ²	90.7 %			76.9 %	

Komplikasyonlar

Table 2. Complications After Pleurectomy Decortication and Extrapleural Pneumonectomy

Author, year	Number of cases P/D, EPP	Complications P/D	Complications EPP
Allen 1994	56, 40	26.8% (15 cases) prolonged air leakage (6), arrhythmias (5), tracheostomy (2), renal failure (2), pneumonia (1)	30% (12 cases); bronchopleural fistula (2), vocal cord paralysis (2), arrhythmias (3), tracheostomy (2), chylothorax (1), MI (1) contralateral benign pleural effusion (1), splenectomy (1), pneumonia (1)
Pass, Kranda 1997; Pass, Temeck 1997	39, 39	Supraventricular tachyarrhythmias (2) Postoperative pancreatitis (4), esophageal-pleural fistula (2), hemorrhage (2), diaphragmatic herniation (1), temporary left radial nerve palsy (1), wound dehiscence (1) ^a	Supraventricular tachyarrhythmias (14), bronchopleural fistulae (7)
Aziz 2002	47, 64	Re-exploration for bleeding (1), pneumonia (1)	21% (14 cases); ARDS (6), pneumonia (4), bleeding (4), reintubation and ventilation (2)
de Vries 2003	29, 17	Empyema (1)	Atelectasis (2), prolonged air-leak (3), discharge with drainage (1), prolonged ventilation (1), large blood transfusion (3)
Rosenzweig 2005	6, 7	Pneumonitis/TE fistula (1), chest tube leak (1)	Thoracic duct leak (1), empyema (1), wound dehiscence (1)
Okada 2008	34, 31	15%; supraventricular arrhythmias (3), respiratory infection (2),	48%; supraventricular arrhythmias (8), respiratory failure (4), respiratory infection (1), bleeding (2), heart hernia (2), bronchial stump insufficiency (2), chylothorax (2), heart failure (1), laryngeal nerve palsy (1)
Schipper 2008	44, 73	4 (9%) bleeding, respiratory failure (1), MI (1)	37 (50.5%); empyema (14), respiratory failure (10), bronchopleural fistulae, bleeding (5), orthostatic hypotension (5), ARDS (4), bowel herniation (4), MI (3), acute renal failure (3), cerebrovascular accident (3), pulmonary embolism (3), cardiac herniation (2), vocal cord paralysis (2), gastric perforation (1), heart failure (1), pleurocutaneous fistulae (1), splenic rupture (1), esophageal perforation (1), delayed gastric emptying (1), metabolic encephalopathy (1), gastrophleural fistula (1)
Borasio 2008	12, 15	33% (4 cases); bleeding (2), atrial fibrillation (1), retained secretions (1)	60% (9 cases); atrial fibrillation (4), respiratory failure (3), bleeding (3), ileus (2), pneumonia (1), vocal cord paralysis (1)
Mineo 2010	44, 27	13.6% (6 cases); bleeding (4), DVT (2)	33% (9 cases); cardiac arrhythmias (4), bleeding (2), vocal cord palsy (1), DVT (2), bronchopleural fistula (2)
Luckraz 2010	90, 49	Atrial fibrillation (8)	Infections (8), bronchopleural fistula (7), atrial fibrillation (2)
Friedberg 2011	14, 14	DVT requiring anticoagulation (4) atrial fibrillation (3), chyle leak (2), pneumonia (3), respiratory failure (1), persistent air leak (1)	DVT requiring anticoagulation (6) atrial fibrillation (3), chyle leak (1), pneumonia (2), respiratory failure (2), pulmonary embolism (1), stroke (1), MI (1)
Rena 2012	37, 40	24% (9 cases); Atrial fibrillation (2), bleeding req operation (1), MI (1)	62% (25 cases); Atrial fibrillation (17), bleeding req operation (2), pneumonia (2), ARDS (1), cerebral ischemic attack (1), pulmonary embolism (1), bronchopleural fistula with empyema (1), gastric hernia after diaphragmatic prosthesis dislocation (1)
Nakas, Waller 2012; Nakas, Meyenfeldt 2012	85, 127	Reoperation (5), prolonged air leak (20), pleural sepsis (5)	Reoperation (19), pleural sepsis (8)

(Continued)

Yorum-1

- Plörektomi/dekortikasyon (P/D) ameliyatı 2 yıllık sağkalımlarda EPP'ye göre istatistiksel olarak anlamlı olmasa da daha iyi gözüküyor.
- Bu çalışma, randomize klinik çalışmanın olmadığı günümüzde 1512 P/D yapılan hasta ile 1391 EPP yapılan olguyu karşılaştırdığı için elimizdeki en iyi verileri sunmaktadır.
- Yine de her bir işlem için farklı seçim kriterlerinin olabileceği unutulmamalıdır.

Yorum -2

- Çalışmanın başka bir kısıtlılığı 7 çalışmanın 2 yıllık sağkalımlar vermiş olmasıdır.
- Çalışmaların bazılarında bazı hastalara ayrıca, fotodinamik tedavi, intraplevral kemoterapi veya intraplevral povidone-iyot tedavisi uygulanmıştır.
- Bu çalışmalarda kemoterapinin yanıt veren olgularda sağkalımı arttırdığı saptanmıştır.

Yorum-3

- Kısıtlılık: 90 günlük mortalite bazı çalışmalarda.
- Çalışmaların bazılarında adjuvan ve indüksiyon tedaviler de kullanılmış.
- Sonuç olarak, plörektomi/dekortikasyon, ekstraplevral pnömonektomiye göre 2.5 kat daha az komplikasyona yol açmaktadır. Bu nedenle plörektomi/dekortikasyon tercih edilmelidir.