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Review

PARADIGM CHANGE IN 30 YEARS PERITONITIS TREATMENT – A REVIEW ON SOURCE CONTROL

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Abstract: Peritonitis remains a hot spot for surgeons despite advancements in surgical technique and intensive care treatment. There is an ongoing interest to improve the survival rate by analyzing the pathogenesis and pathophysiology of this threatening disease.

The significance of source control,e.g., eradication of a focus of infection, elimination of microbial contamination and restoration of local environment, is well recognized since the beginning of the last century. Recently the term "source control" has gained new interest with regard to guidelines for clinical studies. It appears that despite stratification in most clinical peritonitis studies there is still a lack of comparability of those studies with regard to source control. A medline search on peritonitis and source control was performed and 90 studies were evaluated for information on source control evaluation. In summary, there is no uniform definition of source control available. Most studies in peritonitis treatment are according to evidence based medicine level 3-5 evidence. Lack of hard scientific evidence how to measure the success of source control had to be substituted by surgical experience. Re-operation or relaparotomy may be considered as acknowledgment that source control failed. Controversy exists about primary anastomosis in the inflammed peritoneum. Despite all efforts and more patients enrolled in studies to improve surgical treatment of peritonitis in thirty years it is obvious that the mortality rate has decreased only marginally from 40% to 30%. Commonly accepted principles for source control documentation and evaluation should be established and confirmed in multi-center studies before further studies with new compounds are started.

Key words: Peritonitis; Intra-abdominal Infection; Source control; Multi-Organ Failure; Debridement

INTRODUCTION

Peritonitis remains a hot spot for surgeons despite advancements in surgical technique and intensive care treatment. There is an ongoing interest to improve the survival rate by analyzing the pathogenesis and pathophysiology of this threatening disease. In 1916 Poppert classified peritonitis as primary and secondary peritonitis, or as localized and diffuse peritonitis. The significance of source control,e.g., eradication of a focus of infection, elimination of microbial contamination and restoration of local environment, was well recognized [1]. 1889 Mikulicz made the proposal to use the term "diffuse peritonitis" because the classification of peritonitis would be of "enormous practical significance". Open abdomen, lavage and drainage were already known strategies in these days, although the results were not yet satisfying [2]. Source control as the major principle of peritonitis treatment was established by Martin Kirschner in 1926 when he reported a decrease in mortality from 90%% to almost 46% only by applying sound surgical technique: "1. Die Verstopfung der Infektionsquelle; 2. Die Beseitigung des Exsudates; 3. Die Behandlung des Bauchfelles mit Desinfektionsmitteln; 4. Die postoperative Ableitung des Exsudates" [3]. Since the twenties there were many efforts made by surgeons to give guidelines for the treatment of peritonitis, unfortunately without improving prognosis substantially.

Recently the term "source control" has gained new interest with regard to guidelines for clinical studies [4]. It appears that despite stratification in most clinical peritonitis studies there is still a lack of comparability of those studies with regard to source control. Provided source control is the key for treatment success, uniform criteria are urgently needed to describe source control in clinical studies investigating surgical techniques, antibiotics or immune modulators.

In order to investigate the significance of source control in clinical peritonitis studies a medline search was performed using the key words "peritonitis", "intra-abdominal infection", "source control", "debridement", "organ failure" from 1969 to 2001. Review papers were analyzed for references not indicated in the medline search. Papers were then screened for evaluation for source control with regard to the eradication of the focus of infection, elimination of microbial contamination, and restoration of local environment in the peritoneal cavity.

RESULTS

90 studies investigating different surgical treatment techniques in peritonitis published from 1965 to 2001 were obtained and reviewed. In total 10417 patients were included in these studies with an average mortality rate of 25.3% (n = 2638) (Fig. 1). The focus of interest in these studies has changed during the last 30 years of clinical peritonitis research: the study of surgical techniques is followed by the development of scores to make studies comparable and the analysis of organ failure to improve the outcome.

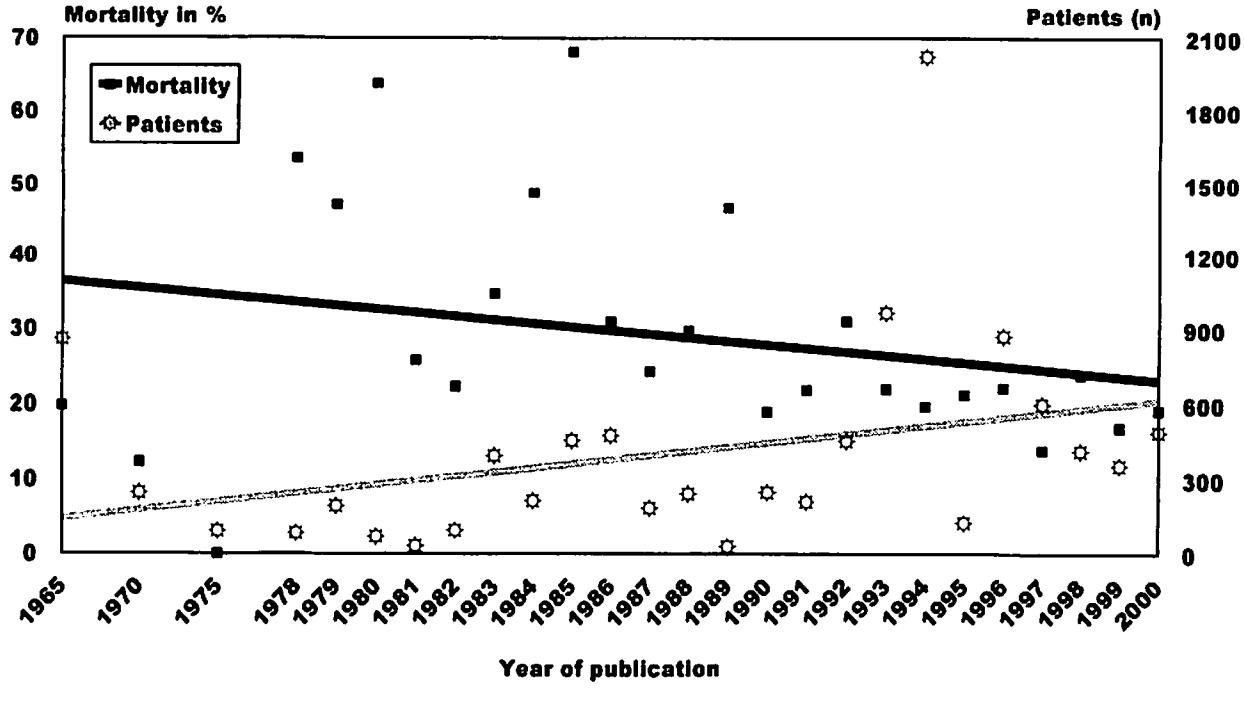

Fig. 1. Year of publication, number of patients and mortality: Trends.

Open Abdomen – Closed Postoperative Lavage – Laparotomy on Demand

The dispute in the seventies is about open abdomen treatment and continuous postoperative lavage. McKenna reported on a prospective study in a series of 50 patients who were treated by continuous postoperative lavage with a mortality rate of 40% [5]. Conventional treatment results are presented in studies by Manelli (1978) and Stephen (1978) in which the mortality rate was 75% and 49%, respectively [6, 7]. A group of French surgeons (Hay, Dupré, Guivarch) and and several North-American surgeons (Steinberg 1979, Duff 1981, Maetani 1981) have retrospectively analysed their open abdomen treatment results with mortality rates between 7% and 54% [8-13]. There were two randomized studies performed: Polk (1980) demonstrated that radical debridement did not cause any benefit to the peritonitis patients [14]. Hunt investigated the significance of irrigation in patients without irrigation, intra-operative irrigation, and intra-operative irrigation followed by continuous postoperative irrigation. The result was quite sobering: irrigation did not improve the mortality rate in peritonitis [15].

Scores – Organ Failure – Risk Factors

In the eighties the discussion focused on organ failure and its importance for outcome in peritonitis. Organ failure may be a risk factor with 80-90% mortality and may be associated with late operation or undrained necrotic tissue or septic foci [16, 17]. The observation that early surgery in organ failure may improve survial lead to the search of sensitive indicators of early organ dysfunction. This was supported by the introduction of statistics into surgical science. Multivariate analysis disclosed that scores (Acute Physiology Score (APS); Acute Physiology and Chronic Health Evaluation Score (APACHE)) co-morbidity, e.g., malnutriton, and age, may predict survival or death in peritonitis. Uniform reporting criteria and pretreatment stratification were proposed for future trials [18, 19]. Management techniques and outcome in severe peritonitis were re-evaluated with the help of the new tools, e.g., statistics, scores, risk factor analysis. High APACHE II score, low serum albumin, and high New York Heart Association cardiac function status were significantly associated with death. Low serum albumin, youth and high APACHE II score were associated with re-operation. However, outcome using different surgical techniques was not different. Closed-abdomen technique and open-abdomen technique had a comparable mortality rate, 31% and 44% respectively [20]. Arthur Baue formulated the target in his editorial in 1975: "What is needed now is to recognize multiple or sequential systems failure as a current problem and study it and define how these sequences or simultaneous events occur and how they might be prevented" [21].

Host Response – SIRS – Organ Support

"The best approach is to prevent the development of organ failure by using sound surgical principles, judgement and techniques, ... removing as much necrotic tissue as possible, improving blood flow and oxygen consumption, supporting nutrition and metabolism, preventing infection or treating it early and

adequately, and excellent organ support. ... Learning more about the feedback loops and control mechanisms of mediators and of inflammation will also better define therapeutic possibilities" [22]. Patients suffering from diffuse peritonitis were treated in sophisticated intensive care units which were prepared to meet most of the above principles. However, it became obvious that new, yet unknown side effects of aggressive treatment emerged. Intensive supportive care of peritonitis patients was considered to lead to the emergence of a new clinical syndrome, tertiary peritonitis, defined as the persistence or recurrence of intraabdominal infection following apparently adequate therapy of primary or secondary peritonitis. This type of peritonitis differs from secondary peritonitis in its microbial flora and lack of response to appropriate surgical and antibiotic therapy [23]. Whereas in the seventies patients with diffuse peritonitis were at risk to die in the immediate perioperative period, ICU-acquired infection in association with progressive organ system dysfunction as an important cause of morbidity and mortality in critical surgical illness occurred days and weeks after the first attempt to eradicate the focus . It was concluded that the host response rather than the microbial attack was responsible for outcome [24] with the gastrointestinal tract as "undrained abscess" providing continuously fuel to the development of multiple organ failure [25, 26]. The specific role of the peritoneal cavity for the immune response in peritonitis has been recognized; peritonitis may be associated with a significant cytokine-mediated inflammatory response that is compartmentalized in the peritoneal cavity. Levels of cytokines may indicate adverse prognosis, may help to stratify peritonitis or guide local therapy [27]. Several attempts were made to use cytokines and immune mediators for outcome analysis and stratification. The combination of scores and cytokine levels, evaluated by multivariate analysis, may predict the mortality with a sensitivity of 84% and a specificity of 90% in surgical intensive care patients [28].

Definition of Source Control

90 papers were then screened for source control definitions or whether source control has been recognized as a significant contribution for the study result. (Table 1). The majority of studies has ignored the necessity of a definition for source control. In 1975 Hudspeth outlined a treatment regimen of radical meticulous surgical treatment of generalized peritonitis which identified the source of contamination, documented the infection, eliminated the source of contamination accompagnied by surgical debridement, recognized complications (bleeding), and indicated an end-point of the treatment: clear effluent, normal appearance of the peritoneum, normalization of body temperature. Intensive supportive therapy, e.g., application of appropriate antibiotics, fluids, electrolytes, whole blood, and ventilatory support, has been emphasized [29]. Polk included a description of conventional treatment and radical debridement in his study with irrigation and a documentation of the infection by cultures. However, management of the primary lesion was left to the discretion of the operating surgeon. There was also no information available on the success of source control, with the exception of in-house mortality [30]. Penninckx reflected on source control in his 1983 paper on planned relaparotomies. Continuous postoperative lavage without adequate peritoneal debridement was not considered successful. Relaparotomies were performed until the abdominal contamination macroscopically disappeared. According to this report complete abdominal reexploration, lavage and drainage were considered mandatory if abdominal and/or general signs of sepsis persiste d or reappeared (on-demand relaparotomy) [31]. Dellinger et al. reported definitions for operative findings, operative procedure, bacteriology and outcome. In this study reasons for re-operations were included: control of the original process, non-infectious complications of the original process, planned operation related to the original process [32].

Andrus et al. committed a study to the evaluation of planned reoperation for generalized intraabdominal infection. Documentation of infection and of the source of contamination was performed. Reoperation was performed if more than 500ml of fluid was present in the abdominal cavity and gram-stain and peritoneal cultures were positive [33].

Cause of intraabdominal sepsis, the time between onset of disease and therapy, intravenous fluid resuscitation, hemodynamic stabilization, alimentary decompression and antibiotics were recorded in a study on open packing of the peritoneal cavity. Operative procedures were repair or excision of the source of contamination, removal of purulent material, and, where appropriate, diversion of the fecal stream [34]. Bartels et al. reported that in 150 patients (82%) source control was successful. In this group mortality rate has been 9% despite successful source control. In case source control was not achieved mortality has been 100% [35]. It is concluded that source control must be achieved during the first operation. Special problems of source control due to anatomical location, e.g., esophagus, duodenum, pancreas, are dealt with. The authors reccommended a prophylactic roux-y-anastomosis in esophageal operations. The results were similar in a study by Billing et al. with a definitive source control in 73/111 patients and a mortality rate of 14% in this group [36].

Resection and stoma were the leading techniques in source control in a study recently published by Büchler, followed by excision and suture, resection and anastomosis, organ resection (appendectomy, cholecystectomy), stoma. Source control has been successful in 166 of 186 (89%) patients. In 20 patients source control was not successful leading to a mortality rate of 25% (n = 5). In 20 patients (115) a continuous postoperative lavage (n = 17) and Etappenlavage (n = 3) has been performed due to failure of primary source control. Mortality rate in this group was 40% (n = 8) [37].

The analysis of failure of source control is seldomly done. Failure to control intra-abdominal infection, abdominal wall necrosis, abdominal bleeding, mechanical ileus, or anastomotic insufficency are just some

Table 1. Clinical studies in patients with severe intra-abdominal infection and peritonitis (no antibiotic study included).

Author	Year	Type of Study	Surgical treatment	Patients	Mortality (%)	Source control Evaluation
Wachsmuth [53]	1965	Retrospective	LD NL	857	19.75	No
Long [54]	1970	Retrospective	Standard treatment	194	5	No
McKenna	1970	Prospective	CPL	50	40	No
Hudspeth	1975	Retrospective	LD radical debridement	92	0	partially
Manelli	1978	Retrospective	LD	16	75	No
Stephen	1978	Retrospective	LD	68	49	No
Champault [55]	1979	Retrospective	OA	27	48	No
Dupré	1979	Retrospective	OA	70	54	No
Guivarch	1979	Retrospective	OA	16	25	No
Hay	1979	Retrospective	OA	64	53	No
Steinberg	1979	Retrospective	OA	14	7	No
Goris [56]	1980	Retrospective	OA	23	50	No
Polk	1980	Randomized	Radical debridement vs standard	46	30	No
Duff	1981	Retrospective	OA	18	39	No
Maetani	1981	Retrospective	OA	13	8	No
Halbfaß [57]	1982	Retrospective	CPL	30	27	No
Hunt	1982	Randomized	NL/IOPL/IOPL+CPL	44	28.5/26.6/33	No
Jennings [58]	1982	Prospective	CPL	20	0	No
Andersson	1983	Open/historic	OA	20	30	Partially
Bohnen	1983	Retrospective	LD	176	38	No
Broome [59]	1983	Retrospective	OA	30	47	No
Pine [60]	1983	Prospective	?	106	27	No
Pennickx	1983	Prospective	PR/LD	42	29/73 (42)	Partially
Wouters [61]	1983	Retrospective	OAMMZ	20	20	No
Hinsdale [62]	1984	Retrospective	Reexploration	119	43	No
Levy [63]	1984	Retrospective	CPL	23	22	No
Sinanan [64]	1984	Retrospective	LD	71	69/81 (67)	No
Bradley [65]	1985	Retrospective	COD/CPD	31	23/44	No
Dellinger	1985	Prospective	LD	187	24	?
Levy [66]	1985	Retrospective	CPL	128	45	No
Machiedo [67]	1985	Retrospective	Re-exploration	50	26	No
Skau [68]	1985	Retrospective	Not indicated	58	28	No
Andrus	1986	Prospective	PR vs LD	77	62/58	Partially
Blum [69]	1986	Retrospective	LD	62	46.8	No
Bunt [70]	1986	Retrospective	Reexploration	93	35.9	No
Chan [71]	1986	Retrospective	OAMMZ	21	29	No
Hallerbäck [72]	1986	Randomized	CPL/LD	79	0	No
Hedderich [73]	1986	Retrospective	OAMMZ	10	20	No
Hünefeld [74]	1986	Retrospective	OPL/CPL/LD	53	23	No
Lambert [75]	1986	Retrospective	LD	105	?	No
Mughal [76]	1986	Retrospective	OA	18	28	No
Teichmann [77]	1986	Retrospective	Etappenlavage	61	22.9	No
Linder [78]	1987	Prospective	?	185	24	No
Bohnen	1988	Retrospective	?	100	31	No
Garcia-Sabrido	1988	Retrospective	OA	15	34	No
Levy [79]	1988	Retrospective	CPL	69	25	No
Schein [80]	1988	Prospective	PR/OA	22	32	No
Walsh [81]	1988	Retrospective	OAMMZ	36	33	No
Ivatury [82]	1989	Retrospective	OA	30	47	No
Penninckx	1990	Retrospective	PR/LD	44	32	No
Schein [83]	1990	Prospective	IOPL	87	17	No
Wittmann [84]	1990	Prospective	Etappenlavage	117	24	No
Bose [85]	1991	Retrospective	OAMMZ	5	60	No
Buanes [86]	1991	Randomized	CPD/LD	83	0	No
Cuesta [87]	1991	Retrospective	OA	24	28	No
Linder [88]	1991	Retrospective	LD/PR	40	35	No
Scholefield [89]	1991	Prospective	PR	6	17	No
Schein [90]	1991	Retrospective	PR/OA	52	44	No
Bartels	1992	Retrospective	PR	184	26	Partially
Billing	1992	Retrospective	PR	152	33.5	Partially
Hakkiluoto [91]	1992	Prospective	OAMMZ	21	52	No
Winkeltau [92]	1992	Retrospective	LD/OA/CPL	96	32	No
Christou	1993	Prospective	OA/CA	239	32	No

Author	Year	Type of Study	Surgical treatment	Patients	Mortality (%)	Source control Evaluation
Demmel	1993	Retrospective	LD/PR	307	15.3	Partially
Ercan [93]	1993	Retrospective	OAMMZ	14	40	No
Nespoli	1993	Retrospective	LD	136	20	No
Ohmann [94]	1993	Prospective	LD/PR	271	21	No
Billing [95]	1994	-	PR vs LD	2003	19.5	No
Hubens [96]	1994	Retrospective	PR	23	39	No
Sugimoto [97]	1994	Prospective	IOPL	101	Not indicated	No
Hau	1995	Prospective	PR/LD	80	21/13	Partially
Schöffel [98]	1995	Prospective	LD	51	27	No
Andersson [99]	1996	Retrospective	PR	60	68	Partially
De Graaf [100]	1996	Retrospective	PR	10	20	No
Götzinger	1996	Retrospective	LD/PR	62	48,1/43	Partially
Koperna	1996	Prospective	LD	92	18.5	Partially
O'Sullivan [101]	1996	Retrospective	Laparoscopic	8	0	No
Seiler [102]	1996	Retrospective	IOPL	161	9.3	No
Teichmann [103]	1996	Retrospective	Etappenlavage	481	18.7	No
Adam [104]	1997	Retrospective	Etappenlavage	30	30	No
Biondo [105]	1997	Prospective	IOCL	212	5	No
Bosscha [106]	1997	Retrospective	PR	50	44	No
Büchler	1997	Retrospective	LD	283	12	Partially
Van Goor [107]	1997	Retrospective	PR	24	29	No
Jiffry [108]	1998	Retrospective	LD/PR	52	23/36.3	No
Kriwanek [109]	1998	Cohort	OA	72	52	No
Navez [110]	1998	Retrospective	Laparoscopic	231	3.9	No
Nathens	1998	Retrospective	LD/PR	59	64	Partially
Wacha [111]	1999	Prospective	LD/PR	355	17	No
Biondo [112]	2000	Retrospective	RPA	127	3	No
Koperna	2000	Retrospective	PR/Re-LD	105	51	Partially
Seiler [113]	2000	Prospective	IOPL	258	14	Partially

CA = closed abdomen
COD = controlled open drainage
CPD = closed postoperative drainage
CPL = closed postoperative lavage
ET = Etappenlavage
IOCL = intra-operative colonic lavage
IOPL = intra-operative lavage
LD = laparotomy on demand
NL = no lavage
OA = open abdomen
OAMMZ = Abdomen Marlex Mesh Zipper
PR = planned relaparotomy
RPA = resection and primary anastomosis

possible reasons which may lead to re-intervention [38].

Failure of source control may be reflected by surgical treatment. Koperna (2000) reported that the source of infection was eradicated in 83 patients leading to a mortality rate of 50.6%. In 22 patients the source was not eradicated and mortality rate was not different (54.5%). The authors defined relaparotomy as celiotomy because of persisting abdominal sepsis [39]. In 29 patients (61.7%) with on-demand revisison source control was successful and mortality rate was 53.2%. 7 patients died despite successful source control. In the group of planned relaparotomy source control has been successful in 11 patients (73.3%), mortality rate was 40% despite successful source control. In case of failure of source control mortality was 100% in both treatment groups [40].

In summary, there is no uniform definition of source control available. Most studies in peritonitis treatment are according to evidence based medicine level 3-5 evidence [41]. It is recognized that the operative approach and the surgical strategy depend on the source of infection, the degree of contamination of the peritoneal cavity, the current condition of the patients and his or her premorbid health status [42]. The general goal of treatment "repair or excision of the source of contamination" has been well accepted [43]. However, in most studies there is no information available how source control was evaluated. Lack of hard scientific evidence how to measure the success of source control had to be substituted by surgical experience [44]. Re-operation or relaparotomy may be considered as acknowledgment that source control failed [45, 46]. Controversy exists about primary anastomosis in the inflammed peritoneum [47]. Postoperative mortality, however, may not differ between colostomy and acute resection [48]. Some authors stated that surgical technique may have no influence on outcome because mortality is related to the severity of peritonitis [49, 50]. In contrast, it has been summarized in a recent review paper that "it is clear that the combination of improved surgical techniques, antimicrobial therapy and intensive care support has improved the outcome of severe secondary peritonitis..." [51]. Despite all efforts and more patients enrolled in studies to improve surgical treatment of peritonitis in thirty years it is obvious that the mortality rate has decreased only marginally from 40% to 30% (Fig. 1). It seems that the missing reduction in mortality may not only be due to the "complexity, chaos and incomprehensibility" of peritonitis, although the offensive in immunology and basic science has not yet

produced clinically relevant results [52]. Commonly accepted principles for source control documentation and evaluation should be established and confirmed in multi-center studies before further studies with new compounds are started.

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