

Abstract.

Immunonutrition and Albumin 20% reduces Complications related to Cystectomy and Nephrectomy Oxidative Stress.

Background.

Major surgeries induce intense oxidative stress and endogenous and exogenous malnutrition, intestine ileus, alteration of immune system and consequently, nosocomial infections, major postoperative complications reduced partially by immunonutrition.(1) Therefore, we aimed to dramatically reduce major postoperative complications after radical cystectomies and nephrectomies by applying a synergistic perioperative antioxidative recovery program based on immunonutrition, in combination with other recovery pathways: physical exercise, iron homeostasis, calory requirement control and, albumin 20% infusion to maintain the crucial protective albumin antioxidant pathway.(2-4)

Methods.

This trial was a multicenter, before-after study. Patients undergoing radical cystectomy and nephrectomy were enrolled into two cohorts: a retrospective cohort (2016 – 2018) and a prospective cohort (2021 – 2025).

We conducted a comparison between historical standard cares and two synergistic Antioxidative and Perioperative Recovery Programs based on immunonutrition, postoperative curative Vialabex albumin 20% infusion (LFB Biomédicaments, Courtaboeuf, France) to maintain serum albumin rate above 35 g/L when a minor or major complication occurred, physical exercise by blowing bubbles in a special bottle providing a positive expiratory pressure (Figure 1), iron homeostasis and calory requirement control (Table 1). Vialabex albumin 20% was 100% pure.

Additionally, dose of albumin 20% infusion was based on hypoalbuminemia range. For 35-25, 24-15 or < 15 g/l, patients received 20, 40 or 60 g/day for 5 days. A control of serum albumin concentration was made at day 6. If the albumin serum concentration was < 35 g/l, a second 5-

days cure of albumin 20% was initiated till the serum albumin concentration reached or overpassed 35 g/l. This protocol was approved by the National Agency of Medication Safety on July 12, 2022.

Figure 2 summarizes the patient care route and flow of the basic recovery program.

	Historical Standard Cares	Program 1	Program 2
Immunonutriton.	None	Pre or postoperatively	Pre AND postoperatively
Curative Albumin 20% infusion if minor or major complication occurred.	None	Only postoperatively	-
Physical Exercise by blowing bubbles in a special bottle providing a positive expiratory pressure.	None	-	Pre AND postoperatively
Calory requirement control.	Occasionally	Pre AND postoperatively	Pre AND postoperatively
Iron homeostasis.	None	Pre AND postoperatively	Pre AND postoperatively

Table 1: Synergistic Antioxidative and Perioperative Recovery Programs based on immunonutrition, postoperative curative albumin 20% infusion when a minor or major complication occurred, physical exercise, iron homeostasis and calory requirement control (35 Cal/kg/day).

Immune-modulating nutrient-enriched product was Oral Impact[®] (Nestlé Health Science, Issy-les-Moulineaux, France), ingested seven to ten days before surgery and pursued or not postoperatively (Table 1).

Likewise, we nevertheless enrolled patients who partially comply with the program like those who have partially taken immunonutrition because of nausea, disgusting taste or difficult glycemia control in the Overall Program 1 group.



Figure 2: Physical exercise by blowing bubbles through a pipe in a special bottle providing a positive expiratory pressure. Bubbles escape by slightly unscrewing the cap. This was made in addition to sitting in an armchair and walking in the surgery setting.

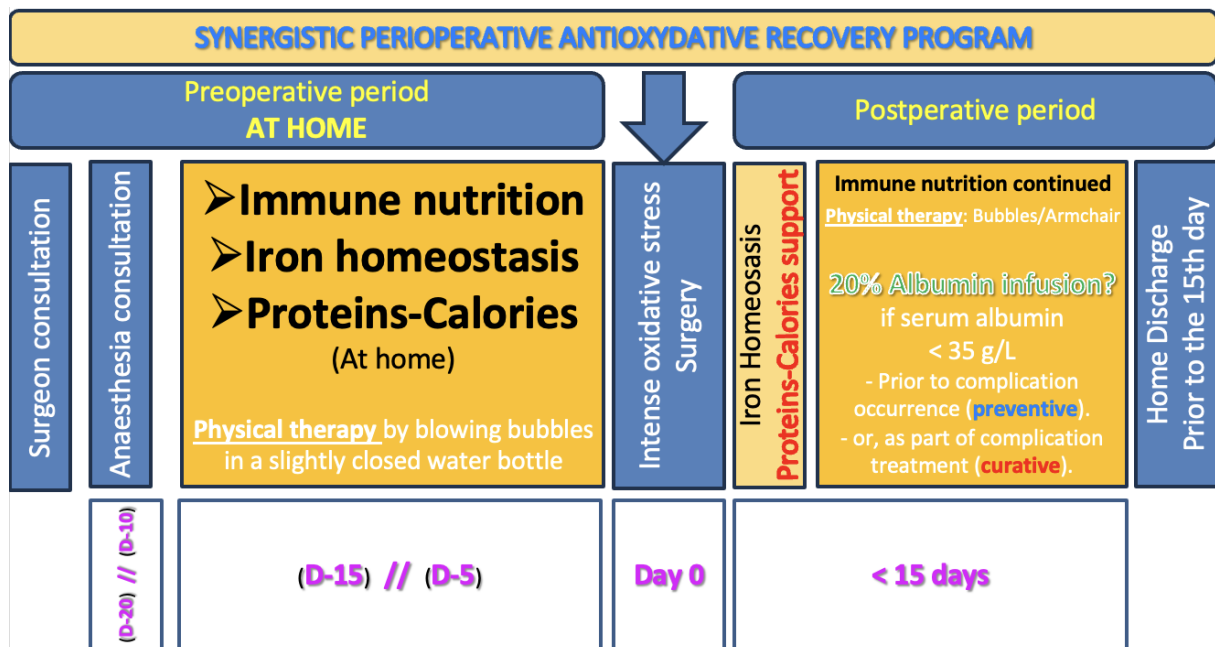


Figure 2: Care route and flow of the synergistic perioperative antioxidative recovery program. D, day.

The main outcome was the rate of major postoperative complications defined by a Clavien-Dindo score ≥ 3 .(5) Secondary outcomes were intensive care unit admissions, mortality, length of stay (LOS), postoperative lowest serum albumin rate, intestine ileus and wound healing delay.

We statistically compared mean $\pm$ standard deviation with the *t* Student test, proportions (number (percentage)) with a khi 2 test and proportion difference with a 95% confidence interval for an alpha error of 0.05.

Results.

	Retrospective Control group	Overall Program 1	Strict Compliance Program 1	Program 2
	N= 107	N = 63	N = 29	N = 22
Age (years)	65.0 $\pm$ 13.4	61.3 $\pm$ 13.3	60.6 $\pm$ 11.8	65.9 $\pm$ 13.5
Weight (kg)	76.4 $\pm$ 18.2	79.6 $\pm$ 20.0	82.2 $\pm$ 20.8	74.4 $\pm$ 15.6
Height (cm)	170.1 $\pm$ 0.1	170.9 $\pm$ 11.0	171.5 $\pm$ 11.6	176.0 $\pm$ 8.2
Gender (male)	82 (76.6)	49 (73.1)	19 (67.9)	12 (54.5)
NRS-2002 (nutritional status)	0.8 $\pm$ 0.9	1.2 $\pm$ 1.3	0.9 $\pm$ 1.3	0.5 $\pm$ 0.8
Preoperative serum albumin rate	-	38.0 $\pm$ 5.0	38.6 $\pm$ 5.5	37.0 $\pm$ 5.3
Nephrectomy	52 (48.6)	44 (63.5)	19 (65.5)	10 (45.4)
Cystectomy	55 (51.4)	23 (36.5)	10 (34.5)	12 (54.6)
Laparoscopy (n)	0	0	0	2

Table 1: Baseline Patient Characteristics.

We enrolled 107 patients who have undergone surgery from 2016 and 2018 in the retrospective control group, 63 patients from 2021 to 2024 receiving prospectively the Program 1 whose 29 complied strictly with it and, finally, 22 patients in 2025 complying strictly with the Program 2.

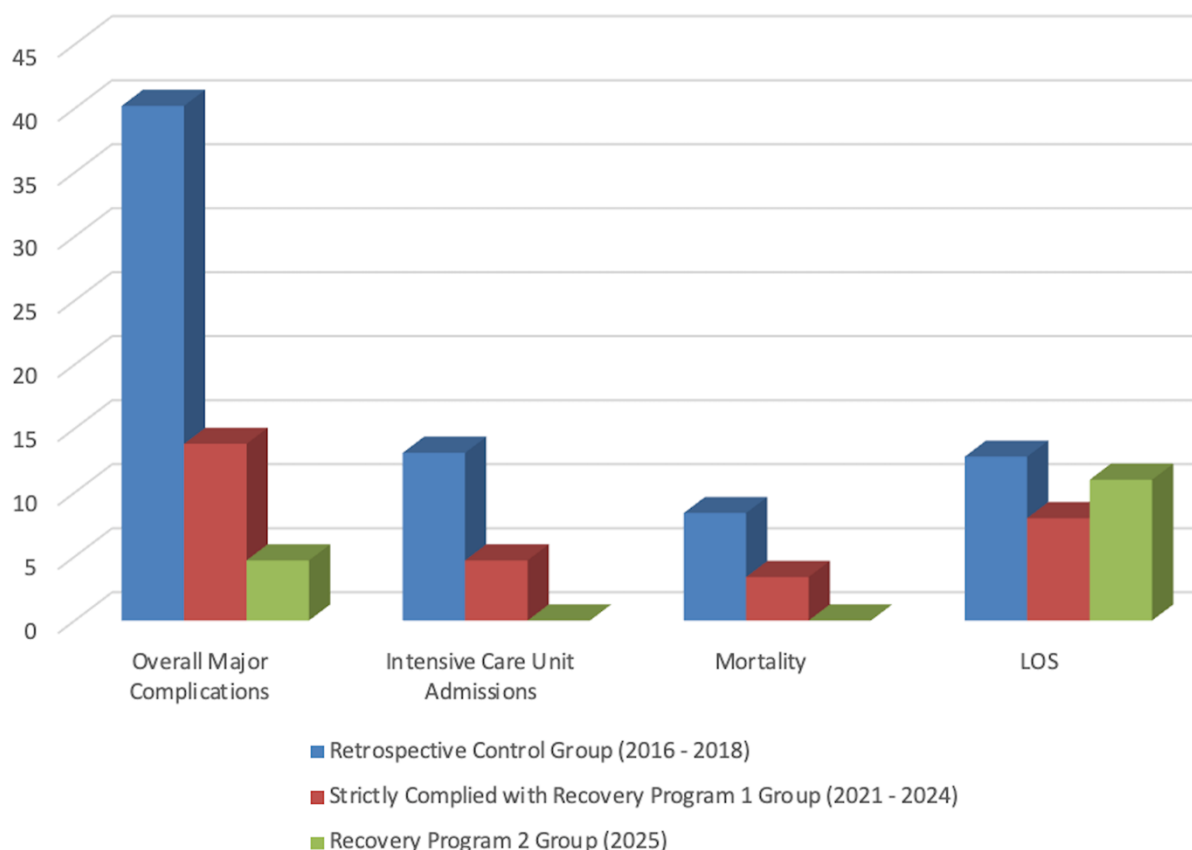


Figure 3: Benefits of a synergistic perioperative antioxidative recovery program on major postoperative complications in patients who underwent radical cystectomy or nephrectomy. LOS, length of stay. Program 1: Immunonutrition only pre or postoperatively, postoperative curative albumin 20% infusion when a minor or major complication occurred. Program 2: Immunonutrition pre and postoperatively, no postoperative albumin 20% infusion, physical exercise. 2 laparoscopies for nephrectomy.

The incidence of major postoperative complications (Clavien-Dindo score ≥ 3) was significantly reduced in the two prospective groups compared to the retrospective control group (Figure 3 and Table 2) as well as in patients who underwent radical cystectomy (Figure 4 and Table 3).

The secondary outcomes are summarized in Tables 2 and 3.

Eleven patients received postoperatively, early albumin 20% infusion in Program 1 group as part of complication treatment, 5 nephrectomies and 6 cystectomies.

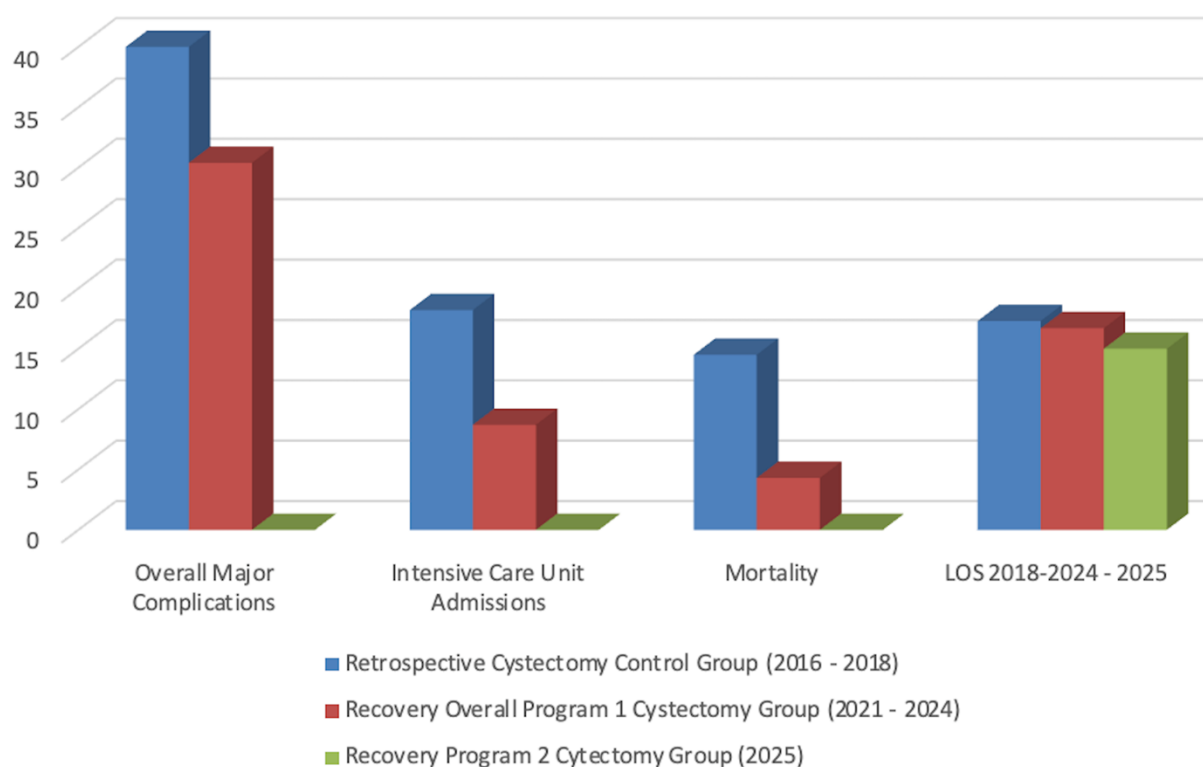


Figure 4: Benefits of a synergistic perioperative antioxidative recovery program on major postoperative complications in patients who underwent radical cystectomy. LOS, length of stay. Program 1: Immunonutrition only pre or postoperatively, postoperative curative albumin 20% infusion when a minor or major complication occurred. Program 2: Immunonutrition pre and postoperatively, no postoperative albumin 20% infusion, physical exercise.

Conclusion.

A strict compliance with a synergistic antioxidant perioperative recovery program based on immunonutrition in combination with other recovery pathways (albumin 20% infusion, iron homeostasis, calory support and physical exercise) can greatly decrease major postoperative complications incidence in patients undergoing radical cystectomy and nephrectomy.

Groups	Retrospective N = 107	Prospective Overall Program 1 N = 63	Strict Compliance with Program 1 N = 29	Prospective Program 2 N = 22
	2016-18	2021-2024		2025
	Standard cares	Pre or postoperative Immunonutrition Curative 20% Albumin infusion	Only Preoperative Immunonutrition Curative 20% Albumin infusion	Pre and postoperative Immunonutrition No Curative 20% Albumin infusion
Major Postoperative Complications (Clavien-Dindo score ≥ 3)	43 (40.2)	11(17.5) Difference = 22.7% IC95 [9.5% – 35.9%] p = 0.0010.*	4 (13.8) Difference = 26.4% IC95 [10.7% – 42.0%] p = 0.010*	1 (4.7) Difference = 35.5% IC95 [22.4% – 46.4%] p = 0.0016*
Postoperative ICU admissions	14 (13.1)	4 (6.5) Difference = 6.6% IC95 [-2.0% – 15.5%] p=0.187	2 (6.8) Difference = 6.3% IC95 [-5.0% – 17.4%] p=0.434	1 (4.7) Difference = 8.4% IC95 [-2.2% – 19.3%] p=0.303
Postoperative Mortality	9 (8.4)	2 (3.0)	1 (3.4)	0 (0.0)
Postoperative LOS (days)	12.8 $\pm$ 7.4	12.0 $\pm$ 8.6 p = 0.250	8.0 $\pm$ 1.3 p = 0.0004*	11.0 $\pm$ 7.4 p = 0.130
Postoperative Intestine Ileus	11 (10.3)	8 (12.7)	3 (10.3)	2 (9.0)
Postoperative wound healing delay	15 (14)	7 (11.1)	4 (13.7)	11 (50) p = 0.00012 ** p = 0.0049 ***
Postoperative lowest serum albumin rate	-	23 $\pm$ 1.5	24.2 $\pm$ 6.1	20 $\pm$ 5.0 p = 0.0057 ** p < 0.001 ***

Table 2: Postoperative outcomes of patients undergoing radical cystectomy and nephrectomy and benefiting from an Antioxidative Perioperative Recovery Program based on immunonutrition, postoperative curative albumin 20% infusion when a minor or major complication occurred, physical exercise, iron homeostasis and calory support. Program 1: Immunonutrition only pre or postoperatively, postoperative curative albumin 20% infusion. Program 2: Immunonutrition pre and postoperatively, no postoperative albumin 20% infusion. ICU, intensive care unit, LOS, length of stay. The study was underpowered to detect a statistical significant difference between group despite a dramatic reduction of postoperative mortality and ICU admissions. *, **, ***, compared to the retrospective group, overall Program 1, Strict compliance with Program 1.

Radical Cystectomy				
Groups	Retrospective N = 55	Prospective Overall Program 1 N = 23	Strict Compliance with Program 1 N = 10	Prospective Program 2 N = 12
	2016-18	2021-2024		2025
	Standard care	Pre or postoperative Immunonutrition Curative 20% Albumin infusion	Only Preoperative Immunonutrition Curative 20% Albumin infusion	Pre and postoperative Immunonutrition No Curative 20% Albumin infusion
Major Postoperative Complications (Clavien-Dindo score ≥ 3)	22 (40.0)	7 (30.4) Difference = 9.6% IC95 [-13.2% – 32.4%] p = 0.420	1 (10.0) Difference = 30.0% IC95 [7.3% – 52.6%] p = 0.049*	0 (0) Difference = 40.0% IC95 [27.0% – 52.9%] P = 0.007*
Postoperative ICU admissions	10(18.2)	2 (8.7%) Difference = 9.5% IC95 [-5.8% – 24.8%] p = 0.289	1 (10%) Difference = 8.2% IC95 [-13.0% – 29.0%] p = 0.460	0 (0) Difference = 18.2% IC95 [7.9% – 28.4%] p = 0.109
Postoperative Mortality	8 (14.5)	1 (4.3)	1 (10.0)	0 (0.0)
Postoperative LOS (days)	17.3 $\pm$ 6.7	16.7 $\pm$ 8.1 p = 0.250	14.9 $\pm$ 5.8 p = 0.146	15.0 $\pm$ 6.4 p = 0.140
Postoperative Intestine Ileus	10 (18.2)	5 (21.7) p = 0.716	1 (10.0) p = 0.525	1 (8.3) p = 0.404
Postoperative wound healing delay	5 (9.1)	4 (17.4)	1 (10)	8 (66.7) p = 0.0012 ** p = 0.0071 ***
Postoperative lowest serum albumin rate	-	24.2 $\pm$ 6.3	23.8 $\pm$ 3.9	20 $\pm$ 3.2 p = 0.0192 ** p < 0.0103 ***

Table 3: Postoperative outcomes of patients undergoing radical cystectomy and benefiting from an Antioxidative Perioperative Recovery Program based on immunonutrition, postoperative curative albumin 20% infusion when a minor or major complication occurred, physical exercise, iron homeostasis and calory support. Program 1: Immunonutrition only pre or postoperatively, postoperative curative albumin 20% infusion. Program 2: Immunonutrition pre and postoperatively, no postoperative albumin 20% infusion, physical exercise. ICU, intensive care unit, LOS, length of stay. The study was underpowered to detect a statistical significant difference between group despite a dramatic reduction of postoperative mortality and ICU admissions. *, compared to the retrospective group. *, **, ***, compared to the retrospective group, overall Program 1, Strict compliance with Program 1.

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