"A PROSPECTIVE SINGLE BLINDED RANDOMIZED CONTROL TRIAL OF PERIOPERATIVE GOAL-DIRECTED FLUID THERAPY VERSUS STANDARD FLUID THERAPY FOR PATIENTS UNDERGOING OPEN RC ON A STANDARDIZED POSTOPERATIVE ENHANCED RECOVERY PATHWAY"

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INTRODUCTION AND OBJECTIVE

- Postoperative ileus (POI) is a common following radical cystectomy (RC)
- Targeted individualized perioperative fluid management has been shown to improve postoperative outcomes and POI for major abdominal surgeries

Arm 1: GDFT
Goal-directed Fluid Therapy

VS

Arm 2: SFT
Standard Fluid Therapy

Primary Endpoint: POI

Secondary Endpoints:
30-day postop complications

METHODS

- 283 pts undergoing open RC/urinary diversion for UCC at MSKCC
- Randomized between 08/2014 and 04/2018 (ClinicalTrials.gov NCT02145871)
- Exclusion criteria: ≤21 yrs old, BMI >45, and active atrial fibrillation
- EV1000 platform with Flotrac Sensor and arterial lines
- Preoperative stroke volume optimization in the GDFT arm
- Protocol fluid optimization was continued in RR for 6 hrs for all pts
- Standardized Enhanced Recovery Pathway for all patients
- Complications collected prospectively to 30 days postop
- No one was lost to FU

PRIMARY TRIAL OUTCOME: POI (POSTOPERATIVE ILEUS)

Defined as :

- Intolerance of oral intake by postoperative day 5
- Required the cessation of diet for abdominal symptoms (distension, NV, excessive burping)
- Placement of a nasogastric tube for clinical signs or symptoms associated with POI, including one or more of the following: nausea, emesis, abdominal bloating or distension, or excessive burping

SELECT PATIENT PREOP CHARACTERISTICS

Characteristics	
Age at surgery (years)	69.4 (63.0-76.0)
Charlson Comorbidity Index	1.0 (0.0-2.0)
CCI adjusted for age	4.0 (3.0-6.0)
ASA 3-4	198 (70%)
BMI at surgery	28.7 (25.4-31.8)
Non-insulin-dependent diabetes	49 (17%)
Insulin-dependent diabetes	12 (4.2%)
Hx of colitis	20 (7.1%)
Prior pelvic surgery (RRP, TAH)	102 (36%)
Hx of prior bowel or abdominal surgery	54 (19%)
Prior abdominal or pelvic radiation therapy	30 (11%)
Received neoadjuvant chemotherapy	124 (44%)

OPERATIVE CHARACTERISTICS

Characteristic	GDFT N=142	SFT N=141
Type of diversion:		
Ileal conduit	85 (60%)	95 (67%)
Neobladder	54 (38%)	45 (32%)
Continent stomal diversion	3 (2.1%)	1 (0.7%)
80mm bowel anastomotic stapler	77 (54%)	62 (44%)
Length of surgery in minutes	319.0 (288.0–352.0)	310.0 (267.0–358.0)
Length of anesthesia in minutes	416.0 (370.0–444.0)	391.0 (337.0–445.0)
Extubated in OR	140 (99%)	138 (98%)
Total EBL (ml)	600.0 (400.0–900.0)	750.0 (500.0–1000.0)
Number of pts transfused in OR	18 (13%)	25 (18%)
Number pts transfused PRBC initial admit	69 (49%)	73 (52%)
Transfused > 4 units PRBC initial admit	3 (2.1%)	7 (5.0%)
Epidural for postop pain control (N=282)	112 (79%)	113 (81%)

FLUID ADMINISTRATION

Operating Room Phase

SFT Arm OR Fluids: Per ERAS

- **Maintenance:** 10 ml/kg/hr of crystalloids
- **Blood loss replaced** 1:1 with albumin and/or PRBC transfusion

GDFT Arm OR Fluids:

- Pre-induction passive leg raise: 250-ml crystalloid boluses based on SV
- Post induction: fluids at 3 ml/kg/hr
- Albumin boluses to maintain SVV < 13%

PACU Phase: 6hr postop

- **SFT arm:** 1.5 ml/kg/hr of crystalloids
- **GDFT arm:** 1 ml/kg/hr of crystalloids
  - A 250 ml crystalloid bolus challenge after the first hour in RR
  - Additional boluses per SV optimization
- All pts received colloid 250-ml boluses for systolic blood pressure <90 mmHg and/or urine output <0.5 ml/kg/hr over 2 hrs

Blood loss was not replaced unless accompanied by an increase in SVV, if hemoglobin <7 mg/dl, if there was hemodynamic instability, and/or active coronary heart disease

Fluid and Vasopressor use in OR	GDFT N=142	SFT N=141	P value
FLUID VOLUMES			
Total Protocol crystalloid (ml)	2892 (2340–3450)	**5580** (4650–6730)	**<0.0001**
Total Protocol colloid (ml)	1000 (750–1500)	975 (500–1350)	0.053
OR crystalloid (ml)	1800 (1400–2220)	**4850** (3800–5900)	**<0.0001**
OR colloid (ml)	**1000** (750–1250)	750 (500–1000)	**0.005**
PACU crystalloid (ml)	**1018** (791–1370)	750 (650–875)	**<0.0001**
PACU colloid (ml)	0 (0–250)	0 (0–250)	0.8
Total fluid intake for hospitalization (ml)	12657 (9912–17280)	13072 (9363–17157)	0.7
Number pts with negative fluid balance	93 (65%)	98 (70%)	0.5
VASOPRESSORS in the OR			
Number pts received ephedrine	82 (58%)	84 (60%)	0.8
Ephedrine (mg)	5.0 (0.0–20.0)	5.0 (0.0–20.0)	0.8
Number pts received phenylephrine	79 (56%)	88 (62%)	0.3
Phenylephrine (mcg)	80.0 (0.0–200.0)	100.0 (0.0–240.0)	0.3

Primary and Secondary Outcomes

Outcomes	GDFT N=142	SFT N=141	P
Primary Outcome:			
Postoperative ileus (POI)	36 (25%)	30 (21%)	0.5
- Required NGT during hospitalization	22 (15%)	23 (16%)	0.9
Secondary Outcomes:			
Total fluid intake during hospitalization (ml)	12657 (9912–17280)	13072 (9363–17157)	0.7
Number transfused in the OR	18 (13%)	25 (18%)	0.2
Number given vasopressors in PACU	4 (2.8%)	7 (5.0%)	0.4
Any complications within 30 days of surgery	**136 (96%)**	125 (89%)	**0.028**
High grade (grade 3-5) complication	21 (15%)	23 (16%)	0.7
Postop acute kidney injury (AKI)	**80(56%)**	56(40%)	**0.006**
Complications post discharge	72 (51%)	69 (49%)	0.8

FREQUENCY OF 30-DAY POSTOPERATIVE COMPLICATIONS

Complication Category	Goal-directed fluid therapy N=142	Standard fluid therapy N=141	P value
Surgical	4 (2.8%)	7 (5.0%)	0.3
Wound	46 (32%)	58 (41%)	0.13
Pulmonary	27 (19%)	29 (21%)	0.7
Neurologic	39 (27%)	25 (18%)	0.050
Genitourinary	84 (59%)	60 (43%)	**0.005**
Infection	39 (27%)	37 (26%)	0.8
Gastrointestinal	55 (39%)	48 (34%)	0.4
Cardiac	31 (22%)	30 (21%)	0.9
Bleeding	54 (38%)	52 (37%)	0.8
Miscellaneous	14 (10%)	15 (11%)	0.8
Thromboembolic	7 (4.9%)	13 (9.2%)	0.2

RESULTS SUMMARY

- **Incidence of POI:** Similar between arms (25% GDFT vs 21% SFT, p=0.5)
- **Incidence Grade 3-5 complications:** Similar between arms (15% GDFT vs 16% SFT, p=0.7)
- **Incidence of any complication:** Higher in the GDFT arm (96% vs 89%, p=0.028)
- **Incidence of Acute kidney injury (AKI):** Higher in the GDFT arm (56% vs 40%, p=0.006); however all recovered to preoperative baseline by 30 days
- **Total Fluid intake** for the hospitalization was similar in both arms
- **Vassopressor use** was similar in both arms

GDFT = Goal directed fluid therapy; SFT= Standard fluid therapy

CONCLUSIONS

- No significant benefit/rate reduction of POI or other high-grade perioperative/postoperative 30-day complications with individualized GDFT versus SFT on an ERAS pathway

- Literature review indicates there still is a need to standardize the definitions of outcomes, better delineate their patient populations, and whether ERAS pathways were utilized for better comparison of outcomes across studies