

Appendix: Supplementary Data

Table 1: Cohort study group description and univariate and multivariable analysis of preoperative risk factors for POI

Variable	Category	Overall n=155		No POI n=99		POI n=56		% POI n=3 6,1	Univariate analysis			Multivariable analysis model with ≤ 5 qualifying parameters			
		n	%	n	%	n	%		p-value	RR for POI	95% CI for RR	p-value	RR for POI	95% CI for RR	
Module A – Patient Demographics															
Age at time of surgery	18–49y	32	20,6	22	22	10	18	31,3	1	Reference					
	50–59y	40	25,8	25	25	15	27	37,5	0,58	1,20	0,63	2,30			
	60–69y	53	34,2	36	36	17	30	32,1	0,94	1,03	0,54	1,96			
	70y+	30	19,4	16	16	14	25	46,7	0,22	1,49	0,79	2,83			
Gender	Male	81	52,3	44	44	37	66	45,7	1	Reference			1	Reference	
	Female	74	47,7	55	56	19	34	25,7	0,013	0,56	0,36	0,89	0,12	0,68	0,41 1,11
Ethnicity	White	108	69,7	65	66	43	77	39,8	1	Reference					
	Black	20	12,9	13	13	7	13	35,0	0,69	0,88	0,46	1,67			
	Indian	19	12,3	15	15	4	7	21,1	0,17	0,53	0,21	1,30			
	Other	8	5,2	6	6	2	4								
Tumour stage	Local	65	41,9	40	40	25	45	38,5	1	Reference					
	Regional	61	39,4	41	41	20	36	32,8	0,51	0,85	0,53	1,37			
	Distant	29	18,7	18	18	11	20	37,9	0,96	0,99	0,56	1,72			
Location of malignancy:	Colon (right) No	131	84,5	84	85	47	84	35,9	1	Reference					
	Colon (right) Yes	24	15,5	15	15	9	16	37,5	0,88	1,05	0,59	1,84			
	Colon (left) No	113	72,9	69	70	44	79	38,9	1	Reference					
	Colon (left) Yes	42	27,1	30	30	12	21	28,6	0,25	0,73	0,43	1,25			
	Colon (rectum) No	65	41,9	44	44	21	38	32,3	1	Reference					
	Colon (rectum) Yes	90	58,1	55	56	35	63	38,9	0,41	1,20	0,78	1,86			
	Synchronous lesion No	154	99,4	98	99	56	100								
	Synchronous lesion Yes	1	0,6	1	1	0	0								
Surgical procedure	Low anterior resection (LAR) (rectal)	81	52,3	50	51	31	55	38,3	0,56	1,13	0,74	1,73			
	Right hemicolectomy (right sided)	22	14,2	14	14	8	14	36,4	0,98	1,01	0,55	1,83			
	Abdominal perineal resection (APR) (rectal)	23	14,8	16	16	7	13	30,4	0,55	0,82	0,43	1,58			
	Other (n<15 per type of surgical procedure)	33	18,7												

Variable	Category	Overall n=155		No POI n=99		POI n=56		% POI n=3 6,1	Univariate analysis			Multivariable analysis model with ≤ 5 qualifying parameters			
		n	%	n	%	n	%		p-value	RR for POI	95% CI for RR	p- value	RR for POI	95% CI for RR	
Surgical access	Open operation	93	60	63	64	30	54	32,3	1	Reference					
	Laparoscopic completed	57	36,8	33	33	24	43	42,1	0,22	1,31	0,85 1,99				
	Laparoscopic assisted open operation	3	1,9	2	2	1	2								
	Laparoscopic converted to open	2	1,3	1	1	1	2								
Stoma Formation	No	56	36,1	37	37	19	34	33,9	1	Reference					
	Yes	99	63,9	62	63	37	66	37,4	0,67	1,10	0,71 1,72				
Cancer-related complication/s at surgery	No	123	79,4	79	80	44	79	35,8	1	Reference					
	Yes	32	20,6	20	20	12	21	37,5	0,86	1,05	0,63 1,74				
Module B – Functional Status															
Body Mass Index (BMI) within 42 days before the surgery	< 25	46	29,7	31	39	15	30	32,6	1	Reference					
	≥ 25	83	53,5	48	61	35	70	42,2	0,30	1,29	0,80 2,10				
	Missing	26	16,8												
Smoking status	Never	84	54,2	59	60	25	45	29,8	1	Reference			1	Reference	
	Current	20	12,9	16	16	4	7	20,0	0,41	0,67	0,26 1,71		0,19	0,53	0,21 1,37
	Previous	51	32,9	24	24	27	48	52,9	0,0069	1,78	1,17 2,70		0,33	1,28	0,78 2,10
Alcohol consumption	Never	44	28,4	28	28	16	29	36,4	1	Reference					
	Current	98	63,2	61	62	37	66	37,8	0,87	1,04	0,65 1,66				
	Previous	13	8,4	10	10	3	5	23,1	0,40	0,63	0,22 1,84				
ASA grading within 42 days before the surgery	Grade I, patient is a completely healthy fit patient.	44	28,4												
	Grade II, patient has mild systemic disease.	43	27,7												
	Grade III, patient has severe systemic disease, not incapacitating	4	2,6												
	Grade IV, patient has incapacitating disease, a constant threat to life	0	0												
	Grade V, a moribund patient who is not expected to live 24 hours with or without the surgery	0	0												
	Missing	64	41,3												

Variable	Category	Overall n=155		No POI n=99		POI n=56		% POI n=3 6,1	Univariate analysis			Multivariable analysis model with ≤ 5 qualifying parameters		
		n	%	n	%	n	%		p-value	RR for POI	95% CI for RR	p- value	RR for POI	95% CI for RR
NYHA classification within 42 days before the surgery	I, no symptoms and no limitation in ordinary physical activity, e.g., shortness of breath when walking, climbing stairs etc.	64	41,3											
	II, mild symptoms and light limitation during ordinary activity	33	21,3											
	III, marked limitation in activity due to symptoms, even during less-than-ordinary activity, e.g., walking short distances	0	0											
	IV, severe limitations. Experience symptoms even at rest	0	0											
	Missing	58	37,4											
Module C – Modified Charlson comorbidity index (modified CCI); Hypertension														
Modified Charlson Comorbidity Index (CCI)	0	93	60,0	56	70	37	71	39,8		1	Reference			
	1	26	16,8	13	16	13	25	38,5	0,89	0,97	0,60 1,55			
	2 or more	13	8,4	11	14	2	4							
	Missing	23	14,8	19		4								
Hypertension	No	83	53,5	50	63	33	63	39,8		1	Reference			
	Yes	49	31,6	30	38	19	37	38,8	0,91	0,98	0,63 1,51			
	Missing	23	14,8	19		4								
Module D – Gastrointestinal medical history														
Duration of symptoms prior to diagnosis	0-1 Month	41	26,8	27	28	14	25	34,1		1	Reference			
	2-4 Month	44	28,8	23	23	21	38	47,7	0,21	1,40	0,83 2,36			
	5-8 Month	36	23,5	25	26	11	20	30,6	0,74	0,89	0,47 1,72			
	9 Months plus	32	20,9	23	23	9	16	28,1	0,59	0,82	0,41 1,66			
	Missing	2	1,3	1		1								
Previous gastrointestinal diagnosis	None	146	94,2	92	93	54	96							
	Irritable bowel syndrome (IBS)	3	1,7											
	Inflammatory bowel disease (IBD)	5	3,4											
	Any (IBS + IBD)	9	5,8	7	7	2	4							
	Unknown	1	0,6											

Variable	Category	Overall n=155		No POI n=99		POI n=56		% POI n=3 6,1	Univariate analysis			Multivariable analysis model with ≤ 5 qualifying parameters		
		n	%	n	%	n	%		p-value	RR for POI	95% CI for RR	p-value	RR for POI	95% CI for RR
Previous abdominal surgery	No	56	36,1	36	40	20	37	35,7		1	Reference			
	Yes	89	57,4	55	60	34	63	38,2	0,76	1,07	0,69 1,66			
	Missing	10	6,5	8		2								
Module E – Pharmacotherapy														
Acute preoperative pharmacotherapy within 180 days before the surgery	Opioids & non-opioid analgesics, N02AJ - M01A	36	28,1	23	29,1	13	26,5	36,1	>0,99	1,00	0,61	1,64		
	Proton pump inhibitors, A02BC	23	18,0	13	16,5	10	20,4							
	Antibacterials for systemic use, J01	21	16,4	10	12,7	11	22,4							
	Drugs for constipation, A06A	21	16,4	15	19,0	6	12,2							
	Hypnotics and sedatives, N05C	12	9,4	8	10,1	4	8,2							
	Opioids chronic, N02A	11	8,6	6	7,6	5	10,2							
	Antiinflammatory and antirheumatic products -non-steroids, M01A	10	7,8	7	8,9	3	6,1							
	Iron preparations, B03A	9	7,0	6	7,6	3	6,1							
	Antispasmodics and anticholinergics in combination with Other drugs, A03ED	6	4,7	4	5,1	2	4,1							
	Antacids, A02A	5	3,9	4	5,1	1	2,0							
	Anxiolytics, N05B	5	3,9	3	3,8	2	4,1							
	Cannabidiol, N03AX24	5	3,9	4	5,1	1	2,0							
	Antidiarrheals -intestinal antiinflammatory/ antiinfective Agents, A07	4	3,1	3	3,8	1	2,0							
	Antihistamines for systemic use, R06A	4	3,1	2	2,5	2	4,1							
	Corticosteroids for systemic use -plain, H02A	3	2,3	3	3,8	0	0,0							
	Vitamin D and analogues, A11CC	3	2,3	1	1,3	2	4,1							
	Multivitamins, combinations, A11A	3	2,3	2	2,5	1	2,0							
	Antiemetics and antinauseants, A04	2	1,6	2	2,5	0	0,0							
	Enoxaparin, B01AB05	2	1,6	2	2,5	0	0,0							
	Antidiarrheal microorganisms, A07FA	2	1,6	2	2,5	0	0,0							
	Potassium chloride, A12BA01	2	1,6	2	2,5	0	0,0							
	Omega-3-triglycerides incl. other esters and acids, C10AX06	2	1,6	1	1,3	1	2,0							
	Ascorbic acid (Vitamin C, plain), A11GA	2	1,6	1	1,3	1	2,0							
Calcium compounds, A02AC	1	0,8	1	1,3	0	0,0								

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		n	%	n	%	n	%		p-value	RR for POI	95% CI for RR	p- value	RR for POI	95% CI for RR	
	Iron in combination with folic acid, B03A	1	0,8	0	0,0	1	2,0								
	Drugs for urinary frequency and incontinence, G04BD	1	0,8	0	0,0	1	2,0								
	Pyridoxine (vit B6), A11HA02	1	0,8	0	0,0	1	2,0								
	Magnesium compounds, A02AA	1	0,8	0	0,0	1	2,0								
	Vitamin B12 and folic acid, B03B	1	0,8	1	1,3	0	0,0								
	Erythropoietin, B03XA01	1	0,8	1	1,3	0	0,0								
	Multivitamins, plain, A11BA	0	0,0	0	0,0	0	0,0								
	vitamin B1 in combination with vitamin B6 and/or vitamin B12, A11DB	0	0,0	0	0,0	0	0,0								
	other	9	7,0	5	6,3	4	8,2								
	none	48	37,5	28	35,4	20	40,8								
	Unknown	27		20		7									
Chronic preoperative pharmacotherapy (refer to definition)	Antihypertensives, C02	42	34,4	26	35,6	16	32,7	38,1	0,75	1,08	0,68	1,70			
	HMG CoA reductase inhibitors, C10AA	38	31,1	21	28,8	17	34,7	44,7	0,19	1,34	0,87	2,08			
	Beta blocking agents, C07A	22	18,0	14	19,2	8	16,3	36,4	0,98	1,01	0,55	1,83			
	Platelet aggregation inhibitors excl. heparin, B01AC	21	17,2	14	19,2	7	14,3	33,3	0,78	0,91	0,48	1,74			
	Blood glucose lowering drugs -excl. in, A10B	18	14,8	9	12,3	9	18,4	50,0	0,15	1,46	0,87	2,44			
	No														
	Yes												0,18	1,37	Reference 0,86 2,17
	Antidepressants, N06A	16	13,1	8	11,0	8	16,3	50,0	0,18	1,45	0,84	2,49			
	Other drugs for obstructive airway diseases – inhalants, R03B	15	12,3	12	16,4	3	6,1	20,0	0,23	0,53	0,19	1,49			
	Diuretics, C03	14	11,5	9	12,3	5	10,2								
	Thyroid hormones, H03AA	10	8,2	6	8,2	4	8,2								
	Allopurinol -combinations, M04AA51	8	6,6	3	4,1	5	10,2								
	Alpha-adrenoreceptor antagonists, C02CA	5	4,1	4	5,5	1	2,0								
	Immunosuppressants, L04	4	3,3	4	5,5	0	0,0								
	Insulins and analogues, A10A	4	3,3	2	2,7	2	4,1								
	Warfarin, B01AA03	4	3,3	3	4,1	1	2,0								
	Anti-parkinson drugs, N04	2	1,6	2	2,7	0	0,0								

Variable	Category	Overall n=155		No POI n=99		POI n=56		% POI n=36,1	Univariate analysis			Multivariable analysis model with ≤ 5 qualifying parameters		
		n	%	n	%	n	%		p-value	RR for POI	95% CI for RR	p-value	RR for POI	95% CI for RR
	Antiarrhythmics, Class I and III, C01B	2	1,6	1	1,4	1	2,0							
	Aminosalicylic acid and similar agents, A07EC	1	0,8	1	1,4	0	0,0							
	Antiepileptics, N03A	1	0,8	0	0,0	1	2,0							
	Antipsychotics, N05A	1	0,8	0	0,0	1	2,0							
	Direct acting antivirals, J05A	1	0,8	0	0,0	1	2,0							
	Anti-estrogens, L02BA	1	0,8	1	1,4	0	0,0							
	Fibrates, C10AB	1	0,8	0	0,0	1	2,0							
	Antiglaucoma preparations and miotics, S01E	1	0,8	1	1,4	0	0,0							
	Progestogens and estrogens in combination, G03F	1	0,8	1	1,4	0	0,0							
	Cardiac glycosides, C01A	1	0,8	1	1,4	0	0,0							
	Proton pump inhibitors, A02BC	0	0,0	0	0,0	0	0,0							
	Direct factor Xa inhibitors, B01AF	0	0,0	0	0,0	0	0,0							
	Other	0	0,0	0	0,0	0	0,0							
	None	28	23,0	16	21,9	12	24,5							
	Unknown	33		26	35,6	7	14,3							
Neoadjuvant chemotherapy (for any time)	No	123	79,35	77	78	46	82	37,4		1	Reference			
	Adjuvant chemotherapy	28								0,90				
	No Chemotherapy	95												
	Yes	32	20,64	22	22	10	18	31,3	0,72		0,50	1,61		
Location of malignancy	Adjuvant- & no chemotherapy	123	79,35	77	78	46	82	37,4		1	Reference			
	Colon right	4	2,58	4	4	0	0							
	Colon left	10	6,45	8	8	2	4							
	Rectum	18	11,62	10	10	8	14	44,4	0,41	1,27	0,72	2,23		
Number of cycles	Adjuvant- & no chemotherapy	123	79,35	77	79	46	87							
	1-6	16	10,32	10	10	6	11							
	8-12	11	7,10	10	10	1	2							
	Missing	5	3,23	2		3								

Variable	Category	Overall n=155		No POI n=99		POI n=56		% POI n=3 6,1	Univariate analysis			Multivariable analysis model with ≤ 5 qualifying parameters			
		n	%	n	%	n	%		p-value	RR for POI	95% CI for RR	p-value	RR for POI	95% CI for RR	
Antineoplastic agent, L01	Adjuvant & no chemotherapy	123	78,85	77	79	46	82	37,4		1	Reference				
	5-FU + folinic acid + oxaliplatin (FOLFOX), L01BC02 + B03BB01 + L01XA03	21	13,46	17	17	4	7	19,0	0,20	0,55	0,22	1,38			
	Capecitabine + oxaliplatin (XELOX), L01BC06 + L01XA03	9	5,77	4	4	5	9								
	Capecitabine (Xeloda), L01BC06	1	0,64	1	1	0	0								
	Folinic acid + 5-FU and irinotecan (FOLFIRI), B03BB01 + L01BC02 + L01XX19	1	0,64	0	0	1	2								
	Capecitabine + irinotecan (XELIRI), L01BC06 + L01XX19	0	0,00	0	0	0	0								
	5 FU, L01BC02	0	0,00	0	0	0	0								
	5 FU + folinic acid (leucovorin), L01BC02 + B03BB01	0	0,00	0	0	0	0								
	Folinic acid + 5-FU + oxaliplatin and irinotecan (FOLFOXIRI), B03BB01 + L01BC02	0	0,00	0	0	0	0								
	TAS-102 + trifluridine/ tipiracil (Lonsurf), L01BC59	0	0,00	0	0	0	0								
	Irinotecan, L01XX19	0	0,00	0	0	0	0								
	Other	0	0,00	0	0	0	0								
	Unknown	1	0,64	1											
Complications and outcome	Adjuvant- & no chemotherapy	123	79,35	77	79	46	85								
	No	24	15,48	16	16	8	15								
	Yes	4	2,58	4	4	0	0								
	Missing	4	2,58	2		2									
Monoclonal antibodies, L01XC	Adjuvant & no chemotherapy	123	79,35	77	79	46	82								
	Bevacizumab (Avastan), L01XC07	12	7,74	8	8	4	7								
	Cetuximab (Erbix), L01XC06	6	3,87	4	4	2	4								
	No monoclonal antibodies	12	7,74	8	8	4	7								
	Missing	2	1,29	2		0									

Variable	Category	Overall n=155		No POI n=99		POI n=56		% POI n=36,1	Univariate analysis			Multivariable analysis model with ≤ 5 qualifying parameters			
		n	%	n	%	n	%		p-value	RR for POI	95% CI for RR	p- value	RR for POI	95% CI for RR	
Chemotherapy course completed	Adjuvant & no chemotherapy	123	79,35	77	80	46	87	37,4		1	Reference				
	Yes	22	14,19	15	16	7	13	31,8	0,80	0,92	0,47 1,79				
	No	4	2,58	4	4	0	0								
	Missing	6	3,87	3		3									
Module F – Neoadjuvant radiation and -chemoradiation															
Radiation therapy within the last 180 days before the surgery	No	117	75,48	70	71	47	84	40,2		1	Reference		1	Reference	
	Adjuvant radiation therapy	0													
	Radiation therapy not within 180 days	9													
	No radiation therapy	108													
	Yes	38	24,52	29	29	9	16	23,7	0,091	0,59	0,32 1,09	0,20	0,66 0,36 1,24		
Location of malignancy (for any time)	No radiation therapy	108	69,68	65	66	43	77								
	Colon right	0	0,00	0	0	0	0								
	Colon left	5	3,23	3	3	2	4								
	Rectum	42	27,10	31	31	11	20								
Intent of radiation within the last 180 days before the surgery	Radiation therapy not with 180 days & no radiation	117	75,48	70	71	47	84	40,2		1	Reference				
	Long course	35	22,58	27	27	8	14	22,9	0,088	0,57	0,30 1,09				
	Short course	2	1,29	1	1	1	2								
	Palliative	1	0,65	1	1	0	0								
Radio-sensitising chemotherapeutic agent used (for any time)	No radiation therapy	108	69,68	65	68	43	78	39,8		1	Reference				
	No	4	2,58	7	7	2	4								
	Yes	34	21,94	24	25	10	18	29,4	0,30	0,74	0,42 1,31				
	Missing	9	5,81	3		1									

Variable	Category	Overall n=155		No POI n=99		POI n=56		% POI n=3 6,1	Univariate analysis			Multivariable analysis model with ≤ 5 qualifying parameters		
		n	%	n	%	n	%		p-value	RR for POI	95% CI for RR	p-value	RR for POI	95% CI for RR
Type of radio-sensitising chemotherapeutic agent used (for any time)	No radiation therapy	108	69,68	65	67	43	80							
	No sensitising agent	4	2,58	7	7	2	4							
	Capecitabine (oral) (Xeloda), L01BC06	18	11,61	13	13	5	9							
	5 FU + folinic acid (leucovorin) (IV), L01BC02 + B03BB01	10	6,45	8	8	2	4							
	5-FU + folinic acid + oxaliplatin (FOLFOX), L01BC02 + B03BB01 + L01XA03	1	0,65	0	0	1	2							
	Folinic acid + 5-FU and irinotecan (FOLFIRI), B03BB01 + L01BC02 + L01XX19	1	0,65	1	1	0	0							
	Oxaliplatin, L01XA03	0	0,0	0	0	0	0							
	Unknown	4		2		2								
Complications within the last 180 days before the surgery	Radiation therapy not with 180 days & no radiation	117	75,48	70	72	47	84							
	No	27	17,42	21	22	6	11							
	Yes	9	5,81	6	6	3	5							
	Missing	2	1,29	2		0								
Type of complication (n=9)	Gastrointestinal tract (GIT)	3	20											
	Genitourinary tract (GUT)	3	20											
	Central nervous system (CNS)	0	0											
	Skin	6	40											
	Haematological	0	0											
	Neutropenia	1	6,67											
	Other	1	6,67											
	Missing	1	6,67											
Radiation therapy within the last 180 days before the surgery completed	No radiation	108	73,97	65	71	43	83	39,8	1	Reference				
	No	0	0	0	0	0	0							
	Yes	36	24,66	27	29	9	17	25,0	0,13	0,62	0,34 1,14	0,20	0,66	0,36 1,24
	Missing	2	1,37	2		0								