Switch Biologics or Pursue Surgery?
Optimizing Clinical Decision Making in the Treatment of Inflammatory Bowel Diseases

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BACKGROUND

- The advent of biologic therapy has transformed the treatment of inflammatory bowel diseases (IBD) and has decreased the need for surgery.

- Though biologic therapy has led to positive response rates for patients, it is difficult to predict the efficacy and durability of a biologic before an alternative therapy is indicated.

- With each failure, patients face the decision to switch biologics or pursue surgery.

AIMS

(1) **Evaluate outcomes of switching biologic therapy or pursuing surgery in patients who fail their first biologic**

(2) **Identify factors that influence these outcomes**

METHODS

- We performed a retrospective chart review of 766 IBD patients who initiated at least one biologic or underwent surgery at our tertiary medical center between 2015-2021.

- Demographics, disease characteristics, treatment pathways, reasons for therapy discontinuation, IBD related surgeries, endoscopic data, and symptom severity scores were abstracted for each patient.

- Treatment pathways following biologic initiation were defined as:
  (1) Maintenance of first biologic
 (2) Switch to alternate biologic
  (3) Undergo surgery

OUTCOMES OF INTEREST

- Primary outcomes were defined as time to initiation of second biologic agent, time to initiation of third biologic agent, and time to initiation of surgery after biologic initiation.

- Secondary outcomes were defined as time to initiation of surgery alone and time to initiation of biologic therapy after surgery.

- For those who switched biologics or pursued surgery, an outcome was defined as **"positive" (not requiring new biologic) or "negative" (requiring new biologic or surgery)** by the last follow-up.

- Proportion and time-to-event analyses were evaluated. Multivariable Cox regression was used to estimate risk of a "negative" outcome based on demographics, disease duration, location, and behavior.

TABLES AND FIGURES

Mean age (years, Standard Deviation (SD))		36.79	15.55
Sex (n, %)	Male	378	49.34%
	Female	388	50.65%
Race (n, %)	Caucasian	561	73.24%
	Black	33	43.08%
	Asian	43	56.14%
	Other	129	16.84%
Smoking	Never	589	76.89%
	Former	138	18.02%
	Current	39	5.09%
BMI (SD)		24.81	5.02
First degree relative with IBD	Yes	66	86.16%
	No	700	91.38%
IBD type	Crohn's Disease	398	51.95%
	Ulcerative Colitis	368	48.04%
Age of onset (years, SD)		28.9	14.59
Disease duration (years, SD)		7.83	9.54
CD location	Ileal	88	24.31%
	Colon	85	23.48%
	Ileocolonic	182	50.28%
	Upper Gastrointestinal	7	19.34%
CD behavior	Inflammatory	173	48.87%
	Stenosing	103	29.10%
	Penetrating	78	22.03%
Perianal disease	Yes	105	27.78%
	No	273	72.22%
UC location	Proctitis	14	4.70%
	Left-sided	107	35.91%
	Extensive	177	59.40%
Extraintestinal Manifestations (EIM)-Uveitis	Yes	21	2.74%
	No	745	97.26%
EIM-Oral ulcers	Yes	43	5.61%
	No	723	94.36%
EIM-Peripheral arthritis	Yes	86	11.23%
	No	680	88.77%
EIM-Axial arthritis	Yes	50	6.53%
	No	716	93.47%
EIM-Dermatologic	Yes	23	3.00%
	No	743	97.00%
EIM-Primary sclerosing cholangitis	Yes	19	2.48%
	No	747	97.52%

Table 1. Demographics and clinical characteristics of the study population
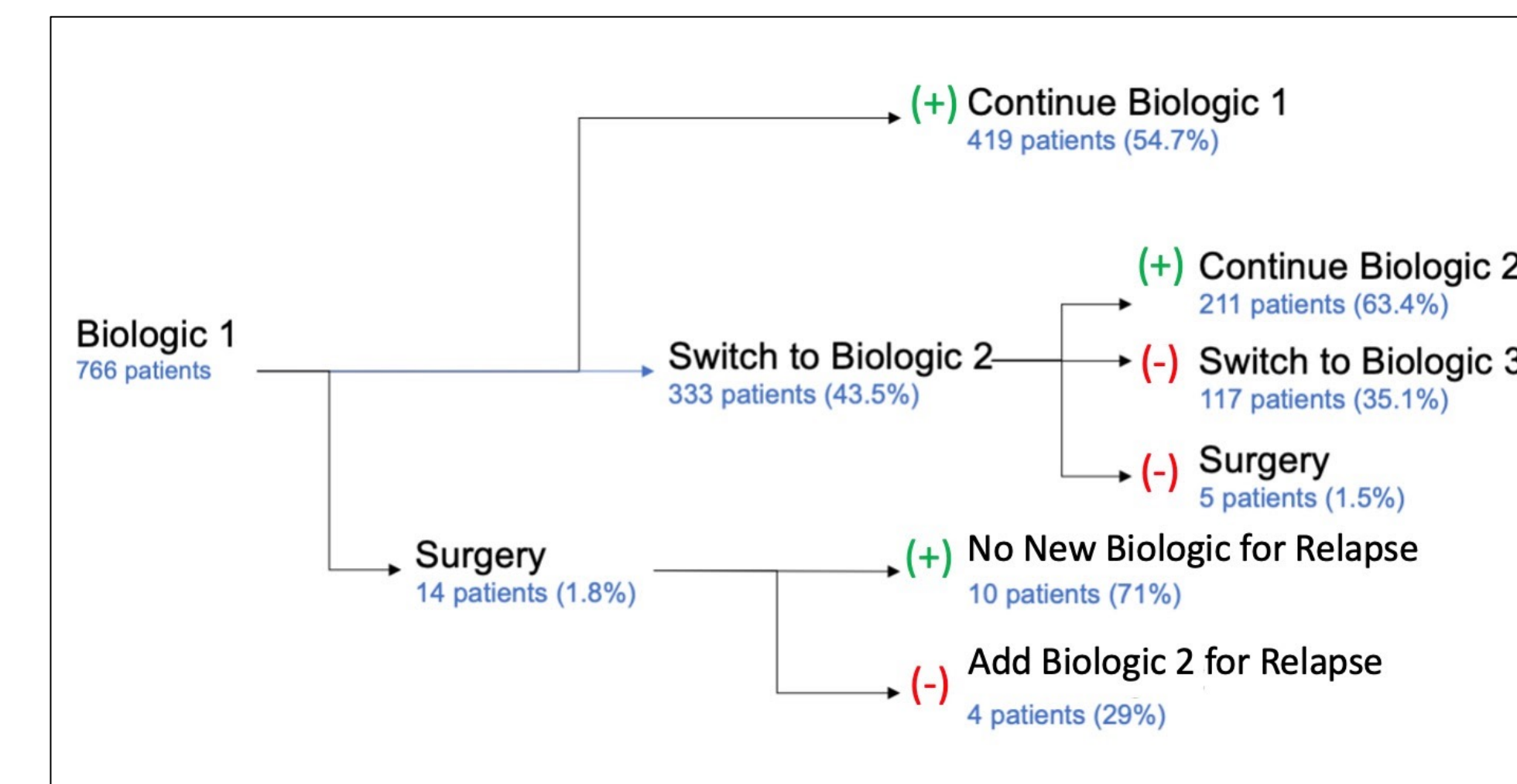
Figure 1. Flow chart outlining the course of treatment for patients with IBD who required initiation of a biologic agent
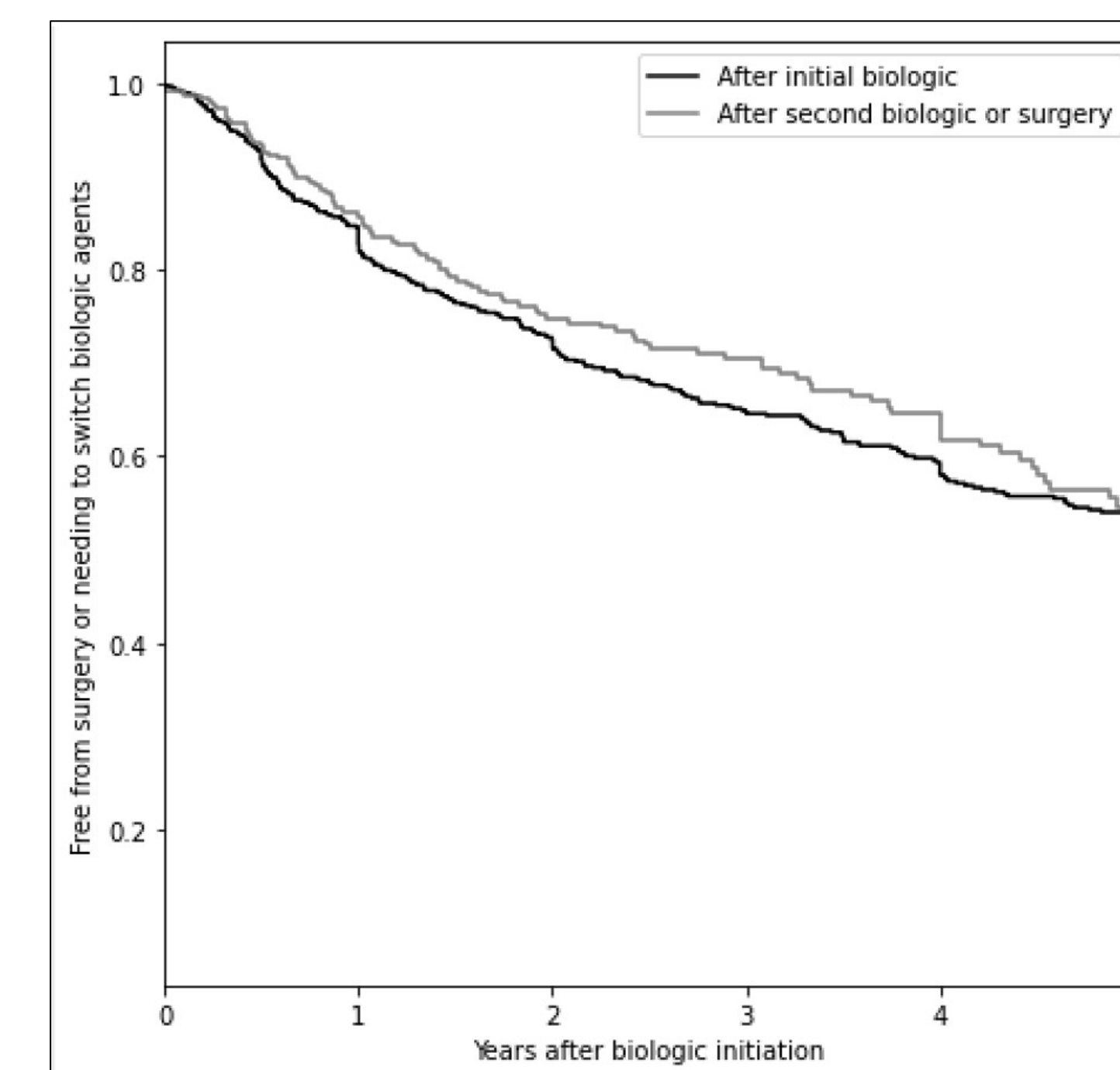
Figure 2. Kaplan-Meier curve of time to switch biologic therapy or need surgery in patients who were treated with a single biologic agent compared to patients who were already treated with a second biologic agent or underwent surgery.

RESULTS

- Patients were followed over a mean time of 5.6 years (+/- 4.2)

- Among those who initiated their first biologic, 54.7% continued the same agent, 43.5% switched to a second biologic agent, and 1.8% underwent surgery.

- The majority of patients who switched to a second biologic or underwent surgery after one biologic ultimately had durable control of disease during the follow-up period comparable to patients who remained on their first biologic (log rank P=0.82).

- Among those who switched to a second biologic, stricturing disease (hazard ratio [HR] 3.44, 95% CI 1.56-7.57) and upper gastrointestinal (GI) involvement (HR 9.98, 95% CI 2.35-42.37) were associated with a "negative" outcome in patients with Crohn's disease (CD).

- For patients with ulcerative colitis, non-white race (HR 1.34, 95% CI 1.06-1.68) was associated with a "negative" outcome.

CONCLUSIONS

- Half of patients had durable control of disease with their first biologic. **For those who failed their first biologic, most switched to a second biologic with durable control of disease thereafter**, while a minority required surgery.

- **CD stenosis, upper GI involvement, and non-white race were risk factors for treatment failure** in patients who switched biologics instead of undergoing surgery.

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