Factors to consider for surgical treatment combined with institution of infliximab therapy in perianal fistula with Crohn’s disease

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Running title: Factors to treat perianal fistula in the Crohn’s disease
The presence of perianal fistula is a common manifestation of Crohn’s disease (CD) and has been reported to be associated with an increased risk of progression to complicated behavior, hospitalization, intestinal resection, and postoperative recurrence [1-3]. The 2005 Montreal World Congress of Gastroenterology decided that the perianal modifier (p) was added in the Montreal classification as a predictor of poor prognosis [4]. Moreover, recent studies showed that long-standing perianal fistula related to CD might be a risk factor for anorectal malignancy [5, 6]. Recent study and meta-analysis showed that perianal fistula in CD is more common in Asian patients than Caucasian patients [7, 8]. From this point of view, treatment strategies for perianal fistula with CD should be established.

A recent population-based study observed that a trend of significantly decreased risk of proctectomy in the biologic era (1998 or after) compared with the pre-biologic era (before 1998), and insisted that this trend reflected the possibility of a disease-modifying effect of biologics on the natural history of perianal fistula in CD [9]. Besides, not only natural course but evidence-based guidelines and reviews also suggested that it was necessary to use anti-tumor necrosis factor (TNF)-α agents for perianal fistula in CD [10-13]. However, there are many factors to consider when using anti-TNF-α agents for perianal fistula in CD, including type of anal fistula (high vs. low or simple vs. complex), presence of proctitis or anal stricture, whether the patient have definite surgical drain or not, use of antibiotics, and timing, dose escalation, and maintenance period of anti-TNF-α agents [10-13].

One among these factors is a start timing of anti-TNF-α agent and several studies investigated the effect of anti-TNF-α agent and described the start timing of anti-TNF-α agent. Based on the findings of several studies, the start timing of anti-TNF-α agent does not seem to matter, consistent with the current study, e.g. although the studies defined the start timing as within 24 hours after surgery, [14, 15] within few weeks after surgery, [16-18] or after the
The current study did not show the type of anal fistula and the presence of combined rectal inflammation or not, and included only seton procedures. Although the anti-TNF-α agent is recommended for the treatment of perianal fistula in CD with high level of evidences [10-13], simple type of perianal fistula in the absence of rectal inflammation may be available for surgical therapy (fistulotomy vs. ligation of internal fistulous tract) without except institution of anti-TNF-α agent [20]. In addition, considering need of maintenance treatment with the anti-TNF-α agent and gradual resistance (resulting in a decreasing efficacy in ~50% of patients over time) [20], a therapeutic strategy of reserving the anti-TNF-α agent is needed for patients with simple type of perianal fistula without proctitis.

Many evidences supported that an appropriate seton drain, followed by anti-TNF-α agent therapy achieved favorable responses regardless of the initiation timing of the anti-TNF-α agent. Further studies for perianal fistula in CD will be needed about the exact evaluation and response method (e.g. van Assche index), timing of response assessment, decision making related to anti-TNF-α agent (e.g. initiation indication, duration, kind of anti-TNF-α agent, dose escalation or change timing), and the timing of seton removal with appropriate method.
References


