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Abnormal Bone Development Related to Irritable Bowel Syndrome and Restrictive Food Intake Disorder

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Bone development is influenced by many factors, including intestinal health and nutrition intake. There is increasing evidence that there is a close connection between intestine health and bone health. Patients with gastrointestinal diseases may exhibit various risk factors for bone diseases, such as intestinal inflammatory activity, corticosteroid therapy, hypogonadism, and nutritional deficiencies. (Lee et al., 2018) Irritable bowel syndrome (IBS) is a common chronic functional gastrointestinal disease that affects more than 10% of the world's population, accompanied by abdominal pain/discomfort, and changes in bowel habits.(Wongtrakul et al., 2020) In addition, avoidance/restrictive food intake disorder (ARFID) was introduced as a condition that restricts nutritional intake due to avoidance or lack of interest in food or diet rather than weight problems, which ultimately leads to clinically significant underweight. (Alberts et al., 2020) Both IBS and ARFID may be affected in bone development, more precisely in bone mineral density, which could lead to some bone diseases, including osteoporosis and osteoporotic fractures. However, gastrointestinal diseases are often overlooked as a cause of osteoporosis or affecting bone mass. (Alberts et al., 2020 ; Lee et al., 2018 ; Wongtrakul et al., 2020)

The exact mechanism of association between gastrointestinal diseases (IBS and ARFID) and bone development is still unclear. Some researchers have hypothesized some possibilities for this mechanism as follows (Fig. 1) : First, intestinal inflammation is one of the factors that accelerate bone mineral loss by releasing inflammatory mediators that promote the increase of osteoclasts and the decrease of osteoblast activity.(Lee et al., 2018) Some pro−inflammatory cytokines, such as interleukin 6, interleukin 8, and TNF−α, are elevated in patients with IBS. (Wongtrakul et al., 2020) Second, the hypothalamic−pituitary−adrenal (HPA) axis is over−activated. Several patients with IBS showed excessive levels of corticotropin (ACTH) and corticosteroids after corticotropin−releasing hormone (CRH). Elevated serum cortisol not only inhibits the proliferation and differentiation of osteoblasts but also inhibits growth hormone and gonadal steroids, resulting in accelerated bone loss. (Wongtrakul et al., 2020)

The nutritional deficiencies were the third possible mechanism. Alberts et al. proposed that the duration of malnutrition in ARFID patients is related to bone mineral density (BMD), even if the body mass index (BMI) remains stable. They hypothesized that a longer duration of underweight in ARFID patients would lead to a decrease in BMD. (Alberts et al., 2020) At the same time, low vitamin D status is one of the common risks of IBS patients, due to some IBS patients avoid dairy products because they believe that they are lactose intolerant or follow a diet designed for IBS patients, as we are known as low−fermentation oligosaccharides, disaccharides, monosaccharides, and polyols (low FODMAP). A diet designed for IBS. This may result in the inability to absorb vitamin D from dietary fats, leading to a higher risk of vitamin D deficiency, which is another risk of osteoporosis or other bone diseases. (Lee et al., 2018 ; Wongtrakul et al., 2020)

Other than that, the fourth possibility is related to the management of IBS patients. The use of selective serotonin reuptake inhibitors (SSRIs), that used in IBS patients, may indirectly influence bone metabolism and increase the risk of osteoporosis and osteoporotic fracture. The SSRI might block the serotonin transporter (5−HTT) in the bone and consequently reduce osteoclast differentiation. (Lee et al., 2018)

Based on the possible mechanisms described above, we need a comprehensive examination of IBS and ARFID pa-

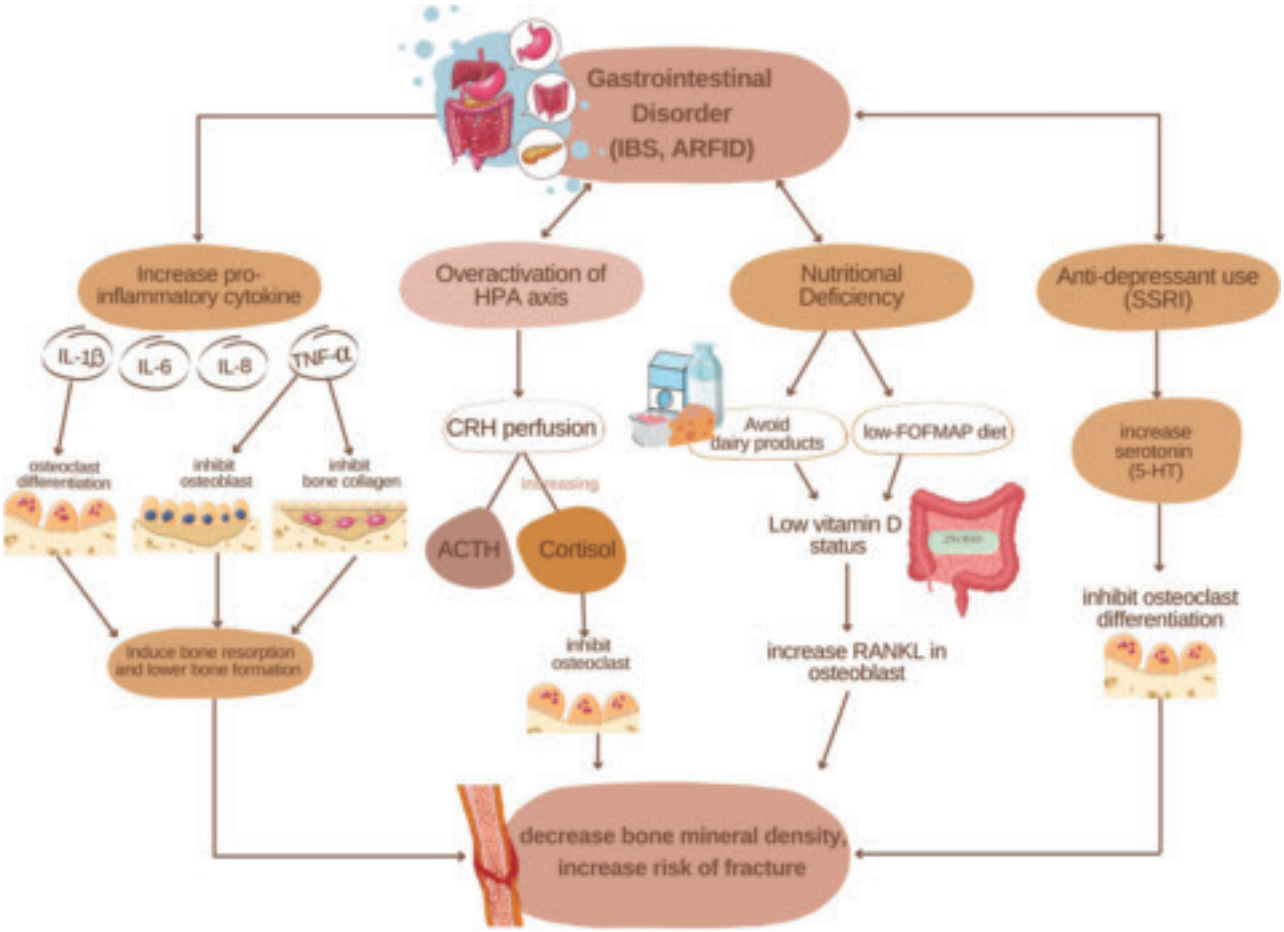

Figure 1. Scheme of several mechanism possibilities for bone disease related to IBS and ARFID patients.
IL−1β : interleukin 1 beta, IL−6 : interleukin 6, IL−8 : interleukin 8, TNF− α : tumor necrosis factor alpha, HPA : hypothalamus, pituitary gland, and adrenal gland, CRH : corticotropin−releasing hormone, ACTH : adrenocorticotropic hormone, Low−FODMAP : low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols, RANKL : receptor activator of nuclear factor kappa−B ligand, SSRI : selective serotonin reuptake inhibitor, 5−HT : 5−hydroxytryptamine.

tients regarding the risk of bone disease, including osteoporosis and fracture risk. Early intervention and counseling for patients with IBS and ARFID are might be applied in the future to determine the risk of bone fracture especially for those who already have other risk factors for bone disease or osteoporosis. The early intervention included measuring the adequate intake of vitamin D and calcium, weight−bearing exercises, and screening the risk of osteoporosis using a bone mineral density scan. Further studies about the mechanism of abnormal bone healing in IBS or ARFID patients are still required to confirm the exact treatment of gastrointestinal disease by not harming bone health, and this might be applied in clinical practice.

References

Alberts Z, Fewtrell M, Nicholls DE, Biassoni L, Easty M, Hudson LD. Bone mineral density in Anorexia nervosa versus avoidant restrictive food intake disorder. Bone, 134, 115307, 2020.

Lee HS, Chen CY, Huang WT, Chang LJ, Chen SCC, Yang HY. Risk of fractures at different anatomic sites in patients with irritable bowel syndrome : a nationwide population−based cohort study. Archives Osteoporos, 13 (1), 80, 2018.

Wongtrakul W, Charoenngam N, Ungprasert P. The association between irritable bowel syndrome and osteoporosis : a systematic review and meta−analysis. Osteoporos Int, 31(6), 1049−1057, 2020.