Summary of Recommendations

1.0 Diagnosis, differential diagnosis, and evaluation

1.1 We suggest that clinicians only make the diagnosis of functional hypothalamic amenorrhea (FHA) after excluding the anatomic or organic pathology of amenorrhea. (Ungraded Good Practice Statement)

1.2 We suggest diagnostic evaluation for FHA in adolescents and women whose menstrual cycle interval persistently exceeds 45 days and/or those who present with amenorrhea for 3 months or more. (2|⊕⊕◯◯)

1.3 We suggest screening patients with FHA for psychological stressors (patients with FHA may be coping with stressors, and stress sensitivity has multiple determinants). (2|⊕⊕⊕◯)

1.4 Once clinicians establish the diagnosis of FHA, we suggest they provide patient education about various menstrual patterns occurring during the recovery phase. We suggest clinicians inform patients that irregular menses do not require immediate evaluation and that menstrual irregularity does not preclude conception. (Ungraded Good Practice Statement)

2.0 Evaluation

2.1 In patients with suspected FHA, we recommend obtaining a detailed personal history with a focus on diet; eating disorders; exercise and athletic training; attitudes, such as perfectionism and high need for social approval; ambitions and expectations for self and others; weight fluctuations; sleep patterns; stressors; mood; menstrual pattern; fractures; and substance abuse. Clinicians should also obtain a thorough family history with attention to eating and reproductive disorders. (Ungraded Good Practice Statement)

2.2 In a patient with suspected FHA, we recommend excluding pregnancy and performing a full physical examination, including a gynecological examination (external, and in selected cases, bimanual), to evaluate the possibility of organic etiologies of amenorrhea. (1|⊕⊕⊕◯)

2.3 In adolescents and women with suspected FHA, we recommend obtaining the following screening laboratory tests: β-human chorionic gonadotropin, complete blood count, electrolytes, glucose, bicarbonate, blood urea nitrogen, creatinine, liver panel, and (when appropriate) sedimentation rate and/or C-reactive protein levels. (1|⊕⊕⊕⊕)

2.4 As part of an initial endocrine evaluation for patients with FHA, we recommend obtaining the following laboratory tests: serum thyroid-stimulating hormone (TSH), free thyroxine (T4), prolactin, luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol (E2), and anti-Müllerian hormone (AMH). Clinicians should obtain total testosterone and dehydroepiandrosterone sulfate (DHEA-S) levels in patients with clinical hyperandrogenism and 8 AM 17-hydroxyprogesterone levels if clinicians suspect late-onset congenital adrenal hyperplasia (CAH). (1|⊕⊕⊕⊕)

2.5 After excluding pregnancy, we suggest administering a progestin challenge in patients with FHA to induce withdrawal bleeding (as an indication of chronic estrogen exposure) and ensure the integrity of the outflow tract. (2|⊕⊕⊕◯)

2.6 We recommend a brain magnetic resonance imaging (MRI) (with pituitary cuts and contrast) in adolescents or women with presumed FHA and a history of severe or persistent headaches; persistent vomiting that is not self-induced; change in vision, thirst, or urination not attributable to other causes; lateralizing neurologic signs; and clinical signs and/or laboratory results that suggest pituitary hormone deficiency or excess. (1|⊕⊕⊕◯)

2.7 We suggest that clinicians obtain a baseline bone mineral density (BMD) measurement by dual-energy X-ray absorptiometry (DXA) from any adolescent or woman with 6 or more months of amenorrhea, and that clinicians obtain it earlier in those patients with a history or suspicion of severe nutritional deficiency, other energy deficit states, and/or skeletal fragility. (2|⊕⊕⊕◯)

2.8 In cases of primary amenorrhea, we suggest evaluating Müllerian tract anomalies (congenital or acquired). Diagnostic options include physical examination, progestin challenge test, abdominal or transvaginal ultrasound, and/or MRI, depending on the context and patient preferences. (2|⊕⊕⊕◯)

2.9 In patients with FHA and underlying polycystic ovary syndrome (PCOS), we suggest:

- a baseline BMD measurement by DXA in those with 6 or more months of amenorrhea and earlier in those with history or suspicion of severe nutritional deficiency, other energy deficit states, and/or skeletal fragility (2/⊕⊕◯◯); and
- clinical monitoring for hyperresponse in those treated with exogenous gonadotropins for infertility. (2|⊕⊕◯◯)

3.0 Treatment of functional hypothalamic amenorrhea and concomitant medical conditions

3.1 We recommend that clinicians evaluate patients for inpatient treatment who have FHA and severe bradycardia, hypotension, orthostasis, and/or electrolyte imbalance. (1|⊕⊕⊕◯)

3.2 In adolescents and women with FHA, we recommend correcting the energy imbalance to improve hypothalamic–pituitary–ovarian (HPO) axis function; this often requires behavioral change. Options for improving energy balance include increased caloric

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