Phenome-wide Comorbidities of Uterine Fibroid Subtypes

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Building Interdisciplinary Research Careers in Women's Health

BACKGROUND

- Uterine leiomyomata (fibroids) are common benign tumors of the uterus with poorly understood etiology
- Prevalence ranges from 20 to 80% by reproductive age
- Common symptoms include abnormal uterine bleeding, pelvic pain, and impacted fertility
- Fibroid locations within uterine wall may have different symptoms and comorbid conditions
- Goal: Identify comorbidity patterns across fibroid structural location subtypes

METHODS

- Selected all adult female participants with uterine fibroids (verified by imaging or pathological report) among those with electronic medical records (EMR) at Vanderbilt University Medical Center
- Using billing codes and free text identified three fibroid subtypes: submucosal, intramural, and subserosal
- Performed phenome-wide association study (PheWAS) of 1,711 PheCodes (diagnoses) for each subtype (cases) compared to other subtypes (controls)
- Logistic regressions for fibroid subtype (outcome) as a function of each PheCode (predictor) were adjusted for age at fibroid diagnosis, reported race, and EMR length

Subtype	N	Mean Age at Dx (yrs)	Race (% Black)	Mean EMR Length (yrs)
Submucosal (SM)	415	41.6	41%	13.1
Intramural (IM)	782	40.9	38%	13.0
Subserosal (SS)	491	40.3	39%	12.6

Table 1. Characteristics of fibroid subtype cases

RESULTS

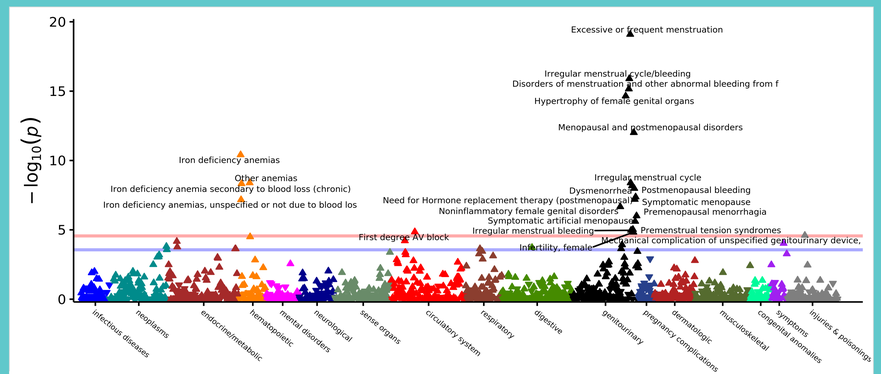

Figure 1. Cross-ancestry PheWAS of submucosal fibroids.
Significance threshold 2.8×10^{-5} (Bonferroni correction)

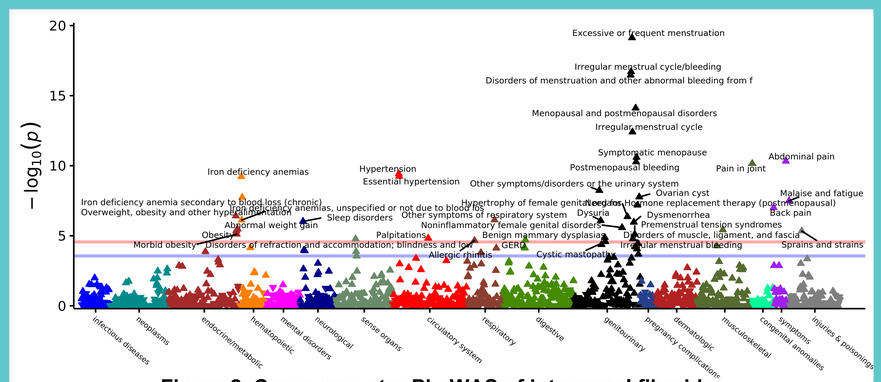

Figure 2. Cross-ancestry PheWAS of intramural fibroids.
Significance threshold 2.8×10^{-5} (Bonferroni correction)

Table 2. Selected PheCode results across fibroid subtypes

Subtypes	PheCode	OR	P-Value
IM, SM, SS	Excessive or frequent menstruation	3.32	7×10^{-20}
IM, SM, SS	Menopausal and postmenopausal disorders	3.34	7×10^{-11}
IM	Hypertension	1.76	4×10^{-10}
SS	Vitamin D deficiency	2.16	2×10^{-8}
IM	Disorders of muscle, ligament, and fascia	5.91	1×10^{-7}
SM	Symptomatic artificial menopause	6.08	2×10^{-6}

RESULTS

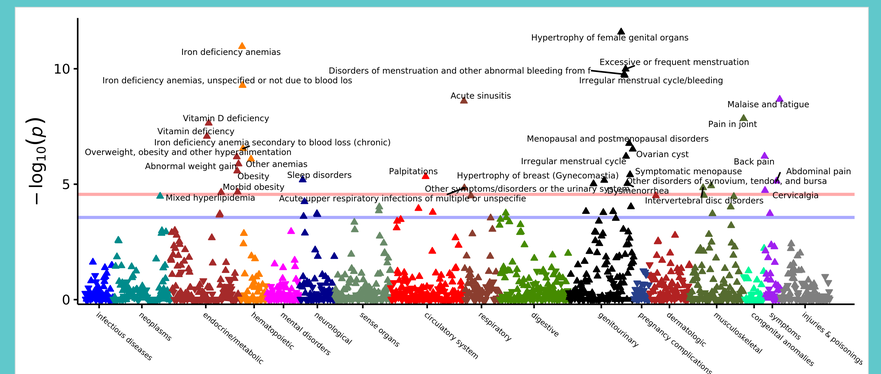

Figure 3. Cross-ancestry PheWAS of subserosal fibroids.
Significance threshold 2.8×10^{-5} (Bonferroni correction)

- 56 PheCodes associated with at least one fibroid subtype
  - 12 codes significantly associated with all three subtypes
  - Excessive/frequent menstruation and irregular menstrual cycle/bleeding
  - Iron deficiency anemias, symptomatic menopause
- Submucosal: 23 significant PheCodes, 5 unique
  - Symptomatic artificial menopause, infertility, premenopausal menorrhagia
  - First degree AV block, Mechanical complication of genitourinary device
- Intramural: 41 significant PheCodes, 12 unique
  - Hypertension, Sprains, muscle disorders, cystic mastopathy, dysuria
- Subserosal: 34 significant PheCodes, 9 unique
  - Vitamin deficiencies, gynecomastia, cervicalgia

CONCLUSION

- Identified consistent associations with menstrual symptoms across subtypes, particularly intramural and submucosal fibroids
- Association of infertility observed only with submucosal fibroids, as well as artificial menopause suggesting an increased risk of hysterectomy with this subtype
- Recapitulated associations with known risk factors across multiple subtypes (i.e. hypertension, vitamin D deficiency, obesity)
- Comorbidity patterns may help develop predictive tools for future fibroids in a subtype-specific manner

This work was supported by funding from TL1TR002244 for JK, K12AR084232 for JNH and from R01HD074711, R03HD078567, R01HD093671 for DRVE.

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