

COLORECTAL CANCER, POLYPS AND RESECTION

Renee Williams, MD, MHPE
Associate Professor of Medicine
Division of Gastroenterology
NYU Grossman School of Medicine
June 4th 2022

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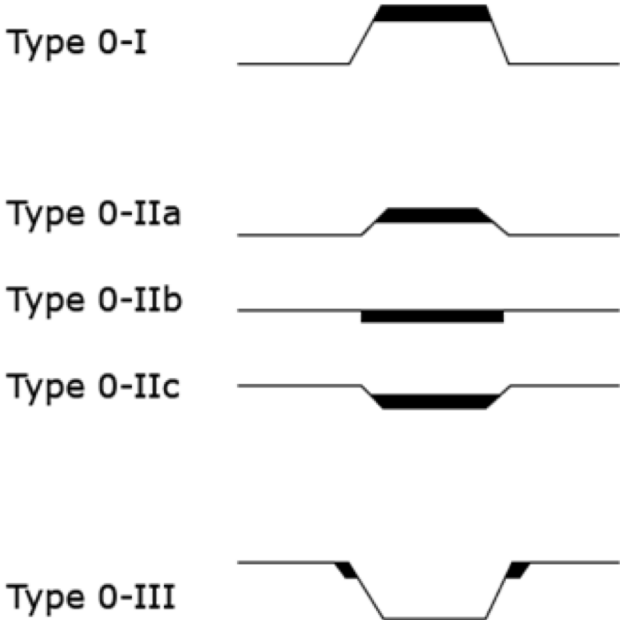
Outline

- ESD vs PM-EMR for Large LSL's
- CONFIRM Trial
- Long term outcomes after ESD
- Cold Snare vs Cold Forceps for Small Polyps – Tiny Polyp Trial

Laterally Spreading Lesions (LSL)

- Endoscopic resection preferred
- No randomized trials between
 - Endoscopic submucosal dissection (ESD)
 - Piecemeal endoscopic mucosal resection (PM-EMR)
- Multi-center, single blinded randomized controlled trial
 - 6 centers, 11 endoscopists
 - ESD vs PM-EMR with snare tip thermal ablation
 - Low risk LSL >25mm
 - Excluded → rectal lesions and pseudo-depressed non-granular LST, O-IIc lesions

Paris classification system of superficial neoplastic lesions of the gastrointestinal tract



Paris classification system of superficial neoplastic lesions of the esophagus, stomach, and colon. Type 0-I lesions are polypoid (protruded or pendunculated); type 0-II lesions are nonpolypoid and may be slightly elevated (IIa), flat (IIb), or slightly depressed (IIc); type 0-III lesions are excavated.

Based on data from: *The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach and colon: November 30 to December 1, 2002. Gastrointest Endosc 2003; 58(6 suppl):S3.*



Outcomes

- Primary
 - Recurrence at 6 months
- Secondary – group comparisons
 - Proportion of R0 resection at one month
 - Cumulative complication rates within 30 days after treatment
 - Proportion of technical failure at day 1
 - Cumulative surgical referral rate over 6 months of follow up

Results

- 359 patients
 - 9/15/2019-10/01/2021
 - ESD 177
 - PM-EMR 182
- 70% of lesions were granular LST
 - mean size 42.9mm (+/- 16.1)
- 60.3% located in the right colon
- 80% of cases were complex

Results

	ESD N=178	PM-EMR N=182	
R0 resection	166(93.8%)	22 (12.1%)	<0.0001
Curative resection	160 (90.4%)	21(11.5%)	<0.0001
Per procedural perforation	10 (5.6%)	4(2.2%)	0.0912
Clinically delayed significant bleeding	14(7.9%)	10(5.5%)	0.3597
Post procedural perforation	1(0.6%)	0(0%)	0.4930
Post polypectomy coagulation syndrome	21(11.9%)	10(5.5%)	0.0317
Duration of the resection	47(30;71)	14.5(10;25)	<0.0001
Duration of anesthesiology	104 (75;133)	66 (52;84)	<0.0001

Conclusions

- ✓ No failure of endoscopic resection
- ✓ ESD superior to PM-EMR in terms of
 - ✓ recurrence rate
 - ✓ R0 resection
 - ✓ Without increasing complications
- ✓ Risk of potentially deleterious loss of pathological information

	ESD (n=178)	PM-EMR (n=182)	
Sessile serrate adenoma	19 (10.7%)	22(12.1%)	0.69
LGD	49(27.7 %)	67(36.8%)	0.06
HGD	62(35%)	55(30.2%)	0.33
Intramucosal carcinoma	34(19.2 %)	30(16.5%)	0.50
Superficial submucosal cancer (<1000µm)	6(3.4%)	1(0.5%)	0.06
Deep submucosal cancer (>1000µm)	7(4%)	7(3.8%)	0.95

CONFIRM Trial

- Randomized controlled trial
- Screening colonoscopy vs annual FIT screening (1:1) randomization
- Average risk adults 50-75 yrs
- Primary outcome: CRC mortality over 10 years
- Recruitment
 - 5/2012-12/2017
 - 46 VA medical centers

CONFIRM Trial: FIT pathway

- US guidelines recommend annual FIT but some countries does biennial FIT
- Aim → determine levels and predictors of longitudinal FIT participation
- Annual FIT+/FIT-
 - Evaluation by site PI for further evaluation (+)
 - 10 year follow up (-)
- Follow up outcomes after 10+ years
 - CRC mortality (primary outcomes)
 - CRC incidence (secondary outcomes)

CONFIRM Trial: FIT pathway

- FIT primer letter mailed 45 days prior to FIT KIT mailing
- FIT participant got verbal and written instructions
- If FIT not returned within 45 days, a second FIT was mailed
- Outcomes
 - Annual -FIT adherence per screening round
 - Biennial – at least once every 2 screening rounds
 - Excluded prior FIT+, anyone with colonoscopy, death within that screening year

Results FIT Adherence

	FIT Completion
Baseline FIT	81.6%
At least 1 FIT (anytime)	87.0%
Exactly 1 of 6	10.6%
Exactly 2 of 6	7.6%
Exactly 3 of 6	6.5%
Exactly 4 of 6	7.1%
Exactly 5 of 6	10.7%
Annual FIT (i.e 6 of 6)	44.5%

Among those eligible for 6 rounds of screening (n=13,893)

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FIT Adherence lower in following groups

- Younger participants
- Black, Hispanic/Latinx participants
- American Indian/Alaska Native participants (biennial only)
- Higher BMI
- Participants with some college
- Current tobacco smokers, those without prior FOBT or colonoscopy

FIT Adherence Positive Association

- Increasing age
- Completing a college degree
- Midwest region
- FOBT or colonoscopy prior to study enrollment

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Conclusions

While initial FIT adherence was initially high (81.6%), adherence fell to 56%-68% in subsequent years

Annual adherence was 44.5%; biennial adherence was 61.1%

Despite annual mailing of FIT, 13% completed screening

- 18.2% completed <3 of 6 screening test

Long-Term Outcomes after ESD for Colorectal Epithelial Neoplasms

- Prospective, large-scale, multicenter cohort trial
- 20 academic centers or tertiary institutions in Japan
- Aims
 - Clarify the long term outcomes of endoscopic submucosal dissection through a large-scale multicenter prospective trial
- 1,883 participants enrolled from 2/2013 to 1/2015
 - ESD on 1,965 neoplasms
 - Neoplastic lesions \geq 20mm extracted for long term analysis

Long-Term Outcomes after ESD

- Primary outcome
 - 5 year survival and intestinal preservation rate
 - Disease specific survival (DSS) and overall survival (OS) rates
 - compared between patients with complete resection (CR) and non-CR lesions
- 1814 lesions \geq 20mm enrolled
- Average tumor size 32.4mm +/- 13.7 mm
- 97% (1759) were removed en-bloc
 - 1640 pathologically curative
 - 174 non-CR of which 111 went to surgery

Results

- 4 disease specific deaths and 74 intercurrent deaths in the 5 year period
- DSS rates higher in CR lesions vs non-CR lesions ($p < .001$)
- OS rates higher in CR lesions vs non-CR lesions ($p = .01$)
- Local recurrence in 8 lesions (0.5%)
 - All were managed endoscopically
- 15 (1%) metachronous invasive CRC's identified at surveillance colonoscopy

	1-year	3-year	5-year
All patients (n=1720)			
Follow up data available (n) %	1640 (95.3)	1511 (87.8)	1208 (70.2)
DSS rate %	100	99.9	99.6
OS rate %	99.6	97.4	93.6
Intestinal preservation rate %	92.7	91.5	88.6
Patients with CR (n=1567)			
Follow up data available (n) %	1493 (95.2)	1368 (87.3)	1085 (69.2)
DSS rate %	100	100	100
OS rate %	99.6	97.6	94.2
Intestinal preservation rate %	99.5	99.0	98.1
Patients with non-CR (n=153)			
Follow up data available (n) %	147 (96.1)	143 (93.5)	123 (80.4)
DSS rate %	100	98.6	96.6
OS rate %	100	95.8	88.6
Intestinal preservation rate %	25.7	22.8	15.2

Conclusion

- Favorable long term outcomes after ESD for treatment of colorectal neoplasms $\geq 20\text{mm}$
- 5 year DSS and OS rates of 99.6% and 93.5%
- Intestinal preservation rate of 98.1% when complete resection achieved in the initial procedure
- *ESD can be a potential first line therapy for superficial colorectal neoplasms $\geq 20\text{mm}$*

Cold Snare vs Cold Forceps for Small Polyps

- USMSTF and ESGE recommends cold snare polypectomy (CSP) for diminutive polyps ($\leq 5\text{mm}$)
- Evidence not clear if CSP is superior over cold forceps polypectomy (CFP) for polyps $\leq 3\text{mm}$
- Single center randomized control trial
- Compared CSP vs CFP for non-pedunculated polyps $\leq 3\text{mm}$

Cold Snare vs Cold Forceps for Small Polyps

- Patients >18 years undergoing colonoscopy
 - Recruited 9/2020-10/2021
- Block randomization for individual polyps during the procedure
 - Two biopsies from polypectomy margin post removal
- Primary outcome non-inferiority for complete resection
 - Defined as absence of polyp tissue at margin biopsies

Results

- 179 patients
 - 106 CSP and 119 CFP
 - 46 patients both CSP and CFP
- Similar demographics across groups
- 279 polyps \leq 3mm
 - 138 CSP
 - 141 CFP

Location of polyp			0.119
Cecum, N (%)	33 (23.9)	27 (19.1)	
Ascending, N (%)	46 (33.3)	37 (26.2)	
Transverse, N (%)	37 (26.8)	35 (24.8)	
Descending, N (%)	10 (7.2)	22 (15.6)	
Sigmoid, N (%)	10 (7.2)	14 (9.9)	
Rectum, N (%)	2 (1.4)	6 (4.3)	

RESULTS

*data available for 130 polyps

**data available for 136 polyps

	Cold Snare n=138	Cold forceps n=141	P value
Mean polyp size, mm (SD)	2.5 (0.5)	2.6 (0.5)	0.161
Pathology			0.009
Tubular adenoma, N (%)	110 (79.7)	93 (66)	
Sessile serrated polyp, N (%)	0 (0.0)	4 (2.8)	
Hyperplastic polyp, N (%)	7 (5.1)	20 (14.2)	
Other non-neoplastic tissue, N (%)	1 (0.7)	4 (2.8)	
Normal colonic mucosa, N (%)	20 (14.5)	20 (14.2)	
Polyp morphology			0.962
Is	129 (93.5)	132 (93.6)	
Ila	9 (6.5)	9 (6.4)	
Positive margin biopsy pathology, N (%)	2 (1.4)	2 (1.4)	0.983
Polyp removed in more than one piece, N (%)	5 (3.6)	22 (15.6)	<0.001
Hemostatic clip used	0 (0.0)	1 (0.7)	0.322
Mean polypectomy time, s (SD)	42.3 (55.5)*	23.2 (23.4)**	<0.001

Conclusion

- *CFP was non-inferior to CSP for complete resection of nonpedunculated polyps $\leq 3\text{mm}$. However CSP required significantly more time to perform compared to CFP.*
- *Based on these results CFP should be considered an acceptable alternative to CSP for the removal of polyps.*

THANK YOU
renee.williams@nyulangone.org

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