

Histopathology of Stenosis Associated with Small Bowel Crohn's Disease: A Systematic Review

SUPPLEMENT

METHODS

The following syntax was applied for the literature search:

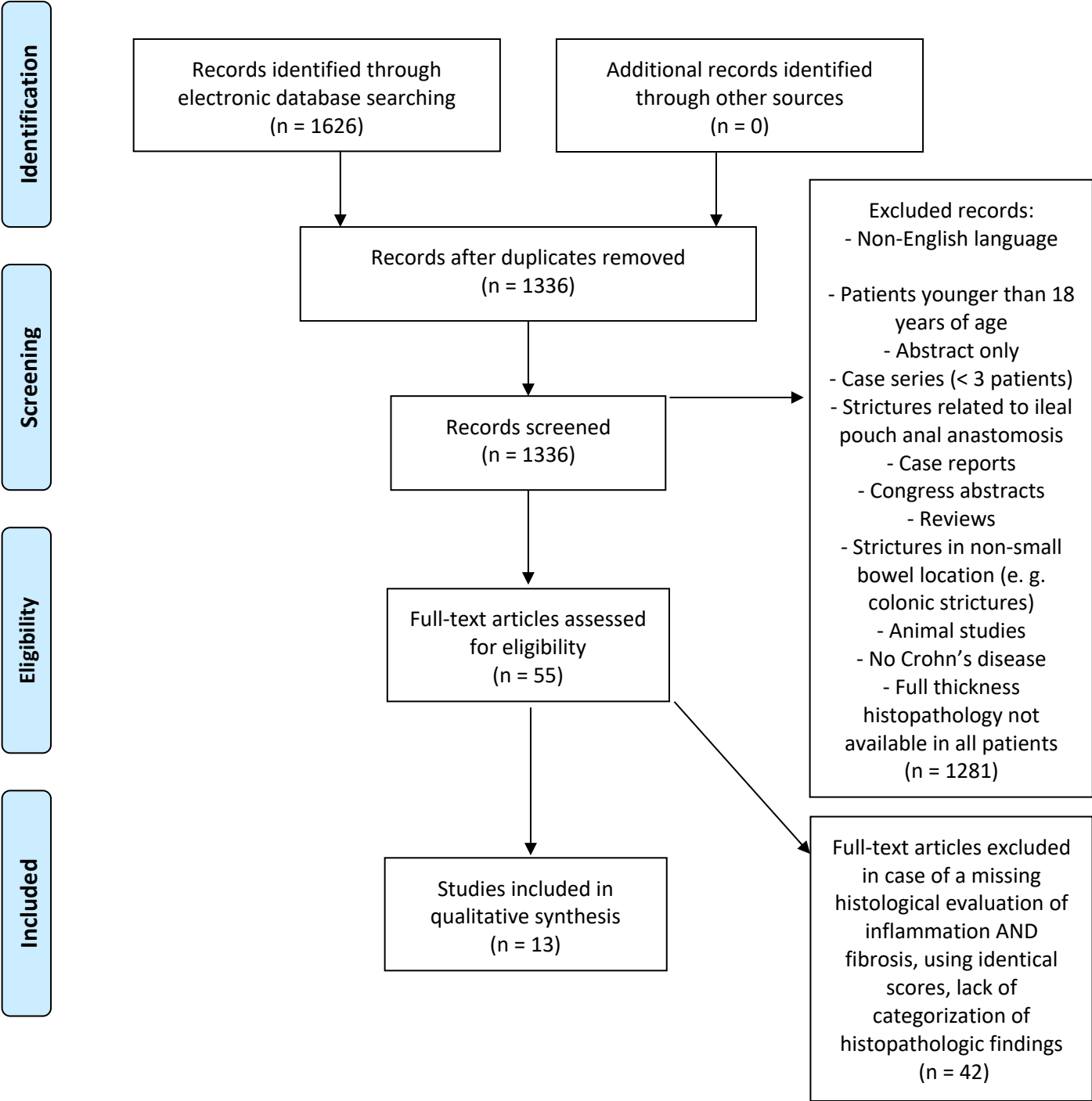
EMBASE (Ovid, 1947-date of search)

1. Crohns disease.mp.
2. Small bowel.mp.
3. dilation.mp.
4. fibrosis.mp.
5. (histology and inflammation).mp.
6. (histology and fibrosis).mp.
7. stricture.mp.
8. OR/3-7
9. 1 AND 2 AND 8

MEDLINE (OVID, 1946-date of search)

Search ((((((dilation) OR (fibrosis) OR ("histology" AND "inflammation") OR ("histology" AND "fibrosis") OR (stricture)))))) AND Small bowel) AND Crohn's disease

Supplementary Figure 1: PRISMA Flow Diagram



Supplemental Table 1: Overall Score Characteristics

Author, year	Focused exclusively on strictured area	Not focused exclusively on strictured area	Assessed stricture and adjacent bowel* in same specimen			
			Yes	No	Probably yes but not explicitly stated	Unknown
Kotanagi, 1991		x			x	
Smedh, 1995		x	x			
Pucilowska, 2000	x				x	
Maconi, 2003	x				x	
Chiorean, 2007		x			x	
Jacene, 2009		x		x		
Zappa, 2011		x			x	
Girlich, 2011		x				x
Adler, 2012	x			x		
Dillman, 2014	x			x		
Pellino, 2016		x				x
Chen, 2017	x		x			
Wagner, 2018		x		x		

* Adjacent bowel indicates non-stricture area from the same surgical specimen.

Supplemental Table 2: Inflammation Score General Characteristics

Author, year	Type of INFLAMMATION scale (can be more than one for different items)					Inflammatory scale includes degree of inflammation only	Inflammatory scale includes depth of inflammation only	Inflammatory scale includes both degree and depth of inflammation	If inflammatory scale includes both degree and depth of inflammation:		
	Dichotomic	Ordinal 3 grade	Ordinal 4 grade	Ordinal 5 grade					Depth separately scored from degree	Depth included in the degree assessment as one score	Depth indicated only by including items such as transmural inflammation or fissuring ulcers
Kotanagi, 1991			X					X			X
Smedh, 1995	X							X	X		
Pucilowska, 2000		X				X					
Maconi, 2003	X		X					X			X
Chiorean, 2007		X						X		X	
Jacene, 2009			X			X					
Zappa, 2011		X						X		X	
Girlich, 2011	X	X						X	X		
Adler, 2012				X			X				
Dillman, 2014				X				X		X	
Pellino, 2016		X				X					
Chen, 2017			X					X	X		
Wagner, 2018	X	X					X				

Supplemental Table 2: Inflammation Score General Characteristics (cont.)

Author, year	Inflammatory scale includes items other than inflammatory cells per se (e.g. crypt distortion, reactive change, edema)	Inflammatory scale only includes inflammatory cells
Kotanagi, 1991	x	
Smedh, 1995	x	
Pucilowska, 2000	x	
Maconi, 2003	x	
Chiorean, 2007		x
Jacene, 2009		x
Zappa, 2011		x
Girlich, 2011	x	
Adler, 2012		x
Dillman, 2014	x	
Pellino, 2016		
Chen, 2017	x	
Wagner, 2018	x	

Supplemental Table 3: Inflammation Score Detailed Characteristics

Author, year	Inflammatory cell terms used						
	Neutrophil	Cryptitis	Crypt abscess	Erosion	Ulcer	Aphthous ulcer	Fissure
Kotanagi, 1991	x	x	x	x	x		x
Smedh, 1995					x		x
Pucilowska, 2000							
Maconi, 2003	x		x	x	x		x
Chiorean, 2007		x	x		x	x	x
Jacene, 2009	x						
Zappa, 2011*	x						
Girlich, 2011	x		x	x			
Adler, 2012							
Dillman, 2014							
Pellino, 2016							
Chen, 2017	x	x	x		x		x
Wagner, 2018	x						

*: categories exclude components of Chiorean scoring system

Supplemental Table 4: Other Score Characteristics

Author, year	Multiple item scales that also include inflammation and fibrosis	Scores limited exclusively to “inflammation” and “fibrosis”	Non-inflammatory cell / non-fibrosis / non-muscle/non-ECM items						
			Edema	Pyloric gland metaplasia	Shortening of villi/villous atrophy	Mucin depletion/ loss of goblet cells	Dilated lymphatics	Surface epithelial damage	Other
Kotanagi, 1991	X		X	X	X	X			
Smedh, 1995	X		X	X	X		X		
Pucilowska, 2000	X							X	
Maconi, 2003	X		X						
Chiorean, 2007		X							
Jacene, 2009	X								
Zappa, 2011		X							
Girlich, 2011	X		X						pseudopolyps, regenerative epithelium, crypt architecture, crypt atrophy, hemorrhage
Adler, 2012	X								
Dillman, 2014		X				X			increased vascular density
Pellino, 2016		X							
Chen, 2017	X								crypt architectural alteration, space volume expansion
Wagner, 2018	X								

Abbreviation: ECM: extracellular matrix

Supplemental Table 5: Fibrosis Score General Characteristics

Author, year	Fibrosis scoring system (can be more than one)					Fibrosis score uses H&E only	Fibrosis score uses other stains	Fibrosis Assessment (only for "fibrosis", regardless of whether a degree scale was applied)	
	Dichotomic	Ordinal 3 grade	Ordinal 4 grade	Ordinal 5 grade	Other			Global score (layer not specified)	Specifies bowel wall layer(s)
Kotanagi, 1991		X				X			X
Smedh, 1995	X				X	X			X
Pucilowska, 2000		X					X		X
Maconi, 2003			X			X			X
Chiorean, 2007		X				X*			X
Jacene, 2009					X		X		X
Zappa, 2011		X				X			X
Girlich, 2011	X					X*		X	
Adler, 2012	X			X		X			X
Dillman, 2014			X				X		X
Pellino, 2016		X				X*		X	
Chen, 2017			X				X	X	X
Wagner, 2018					X		X		X

*Inferred

Supplemental Table 6: Fibrosis Score Detailed Characteristics

Author, year	Fibrosis score includes muscle hyperplasia/hypertrophy element	Fibrosis score only includes fibrosis	Specific fibrosis items						
			(Mentions fibrosis in this layer)						
			Mucosa	Muscularis mucosa	Submucosa	Muscularis propria	Subserosa	Transmural fibrosis/scar	Fibrosis NOS
Kotanagi, 1991		X		X	X				
Smedh, 1995	X				X	X	X		
Pucilowska, 2000	X								X
Maconi, 2003		X		X	X				
Chiorean, 2007	X				X			X	
Jacene, 2009	X*					X			
Zappa, 2011		X			X			X	
Girlich, 2011		X							X
Adler, 2012	X				X	X	X	X	
Dillman, 2014		X	X		X			X	
Pellino, 2016		X							X
Chen, 2017	X*#		X		X	X	X		X
Wagner, 2018	X								X

Abbreviation: NOS: Not otherwise specified

Note: Elements of muscle hypertrophy* and of muscle hyperplasia# are evaluated separately from fibrosis.

Supplemental Table 6: Fibrosis Score Detailed Characteristics (cont.)

Author, year	Muscle items other than fibrosis				Items other than fibrosis or muscle	
	Muscularis mucosa thickened	Muscularis propria thickened	Muscle hyperplasia (MM, MP, or NOS)	Muscle hypertrophy (MM, MP, or NOS)	Neuronal hyperplasia	Other ECM alteration
Kotanagi, 1991					x	
Smedh, 1995	x					
Pucilowska, 2000		x				
Maconi, 2003						
Chiorean, 2007			x (NOS)			
Jacene, 2009		x				
Zappa, 2011						
Girlich, 2011						
Adler, 2012		x				
Dillman, 2014						
Pellino, 2016						
Chen, 2017			x (MM)	x(MP)	x	adipocyte hyperplasia
Wagner, 2018				x(NOS)		

Abbreviations: MM: muscularis mucosa; MP: muscularis propria; NOS: not otherwise specified; ECM: extracellular matrix