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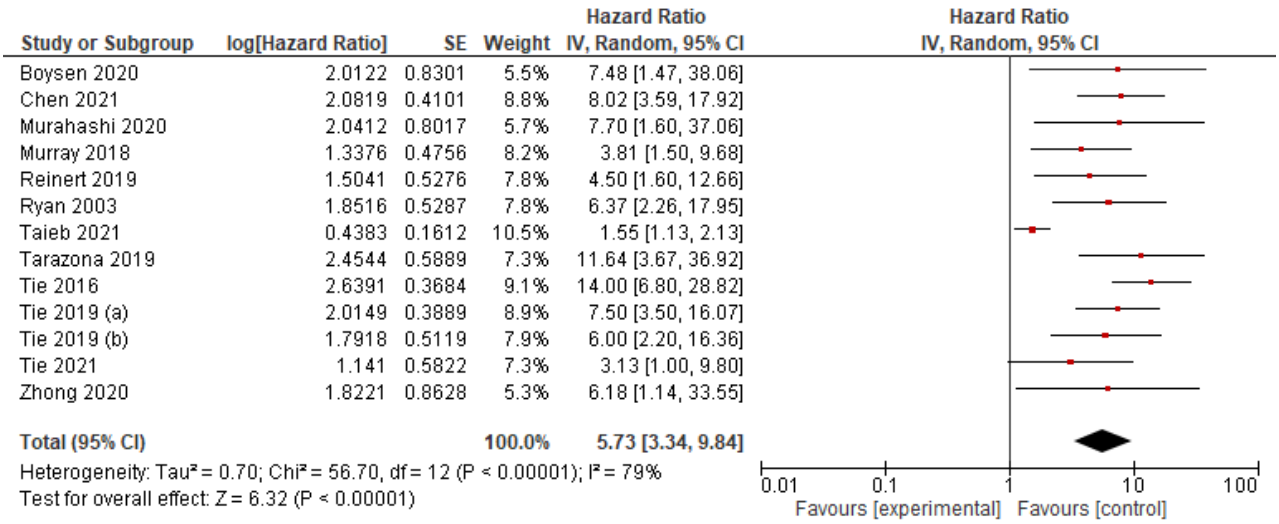
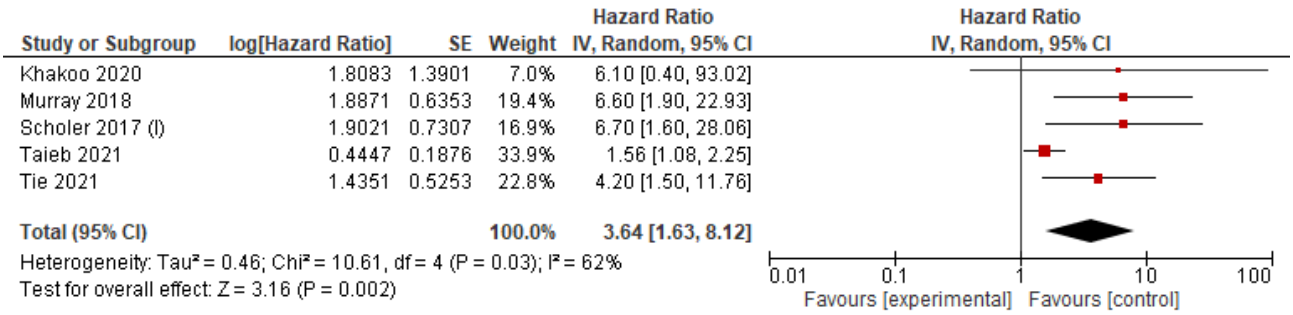


Supplementary Figure 1. Forest plot showing meta-analysis for PFS according to post-operative ctDNA in patients undergoing curative surgical resection for colorectal cancer where multivariate analysis was performed. Data displayed as HR with 95% confidence intervals on a logarithmic scale. HR- hazard ratio PFS- progression-free survival SE-standard error.



Supplementary Figure 2. Forest plot showing meta-analysis for OS according to post-operative ctDNA in patients undergoing curative surgical resection for colorectal cancer. Data displayed as HR with 95% confidence intervals on a logarithmic scale. HR- hazard ratio OS-overall survival SE-standard error.

Pre-intervention	
Bias due to confounding	Q2, Q4, Q5, Q10
Bias in the selection of participants into the study	Q2, timeline (collected in data extraction)
At intervention	
Bias in the classification of interventions	Q6, Q7, Q8
Post-intervention	
Bias due to deviation from intended interventions	Q5
Bias due to missing data	Q9
Bias in the measurement outcomes	Q12
Bias in the selection of the reported results	Q13
Supplementary table 1. Quality Assessment domains. Table to show the mapping of the Quality Assessment proforma used to the domains of bias of the ROBINS-I tool.	

Author	Year	Reason for exclusion	Reference
Appelt	2020	Outcomes reported according to pre-operative ctDNA and ctDNA was not measured after surgery	(1)
Baumgartner	2018	Outcomes reported according to pre-operative ctDNA and ctDNA was not measured after surgery	(2)
Bazan	2006	Outcomes reported according to pre-operative ctDNA and ctDNA was not measured after surgery	(3)
Bidard	2019	Outcomes reported according to pre-operative ctDNA and ctDNA was not measured after surgery	(3)
Boysen	2017	Outcomes reported according to pre-operative ctDNA and ctDNA was not measured after surgery	(4)
Cassinotti	2013	Does not report the proportion of patients with disease relapse, do not report the proportion of patients classified as ctDNA positive after surgery	(5)
Frattini	2006	Outcomes not presented in terms of ctDNA after surgery	(6)
Frattini	2008	Does not give long-term outcomes according to post surgery ctDNA, authors contacted no reply	(7)
Garcia-Olmo	2012	Does not give PFS according to post surgery ctDNA	(8)
Hao	2014	Unable to differentiate surgical patients from non-surgical patients, disease relapse not reported	(9)
Hendricks	2018	Measures CTC not ctDNA	(10)
Herbst	2009	Outcomes reported according to pre-operative ctDNA and ctDNA was not measured after surgery	(11)
Hsieh	2005	Outcomes reported according to pre-operative ctDNA and ctDNA was not measured after surgery	(12)
Iwai	2019	Measures cfDNA not ctDNA	(13)
Li	2020	Only a single patient in their sample underwent surgery for CRC	(14)
Lin	2014	Outcomes reported according to pre-operative ctDNA and ctDNA was not measured after surgery	(15)
Narayan	2019	Outcomes reported according to pre-operative ctDNA and ctDNA was not measured after surgery	(16)
Pazdirek	2020	Outcomes reported according to pre-operative ctDNA and ctDNA was not measured after surgery	(17)
Polivka	2020	Outcomes not presented in terms of ctDNA after surgery	(18)
Schou	2018	Measures cfDNA not ctDNA	(19)
Symonds	2018	Patients not followed up after surgery	(20)
Vidal	2021	Outcomes reported according to pre-operative ctDNA and ctDNA was not measured after surgery	(21)
Vietsch	2018	Wrong study population: retrospectively selected patients who had disease relapse	(22)
Wang	2004	Outcomes not presented in terms of ctDNA after surgery	(23)
Wang	2019	Outcomes presented in terms of ctDNA status during follow-up rather than post-operatively	(24)
Wong	2019	ctDNA analysis in the cohort was not performed routinely post-surgery but at time of concern of disease progression from CT, does not address the issue of MRD	(25)
Yeh	2020	Disease relapse and survival not measured during the follow-up period	(26)
Zhu	2021	Measures cfDNA not ctDNA, no long term follow-up	(27)
Zhong	2020	Measures cfDNA not ctDNA	(28)

Supplementary Table 2. Key excluded studies. Table to show the main excluded studies and reason for exclusion from the review. cfDNA- cell free DNA CTC- circulating tumour cells ctDNA- circulating tumour DNA CRC- colorectal cancer MRD- minimal residual disease

Study ID	Median Survival (months)		Univariate			Multivariate		
	ctDNA positive	ctDNA negative	Hazard ratio	Confidence interval	p value	Hazard ratio	Confidence interval	p value
He 2020	not reached	not reached	not stated	not stated	not stated	-	-	-
Ji 2021	not reached	not reached	not stated	not stated	0.529	-	-	-
Khakoo 2020	not stated	not stated	6.1	0.4-97.1	0.2	-	-	-
López-Rojo 2020	22.8	35.4	-	-	-	-	-	-
Mason 2021 (>4 mutations)	[41% at 2 years]	[96% at 2 years]	not stated	not stated	<0.001	6.60	2.07-21.06	0.001
Murray 2018	Not stated	Not stated	6.6	1.9-22.8	0.011	-	-	-
Scøhler 2017 **(**Primary resection)	Not stated	Not stated	6.7	1.6-28.7	0.01	-	-	-
Taieb 2021	[81% at 5 years]	[87% at 5 years]	1.56	1.08-2.26	0.018	1.65	1.12-2.43	0.0108
Tie 2021	[31.7% at 5 years]	[77.7% at 5 years]	4.2	1.5-11.8	<0.001	-	-	-

Supplementary Table 3. Overall Survival. Table to show time-to-death following surgery according to post surgery ctDNA status. Confidence intervals displayed as 95%CI. CI- confidence interval. HR- hazard ratio.

Study ID	Centre number	Power calculations	Adjustment	Patient population	Co-interventions	Management	ctDNA methodology	Cut-off value	Timeline consistency	Attrition	Blinding	Relapse definition	Selective reporting	Timeline	Attrition (%)	Total
Allegretti 2020	Single	Nil	Nil	High	High	Low	Low	Low	Low	Low	Low	Low	High	Prospective	16.7	8
Beagan 2020	Single	Nil	Nil	Low	High	Low	Low	Low	High	Low	High	Low	Low	Prospective	0	7
Benešová 2019	Multicentre	Nil	Nil	High	High	Low	Low	Low	Low	Low	High	High	Low	Prospective	7.1	8
Boysen 2020	Single	Nil	Performed	Low	Low	Low	Low	Low	Low	Low	High	High	Low	Prospective	0	8
Carpinetti 2015	Single	Nil	Nil	High	Low	Low	High	Low	High	Low	Low	Low	Low	Prospective	0	8
Chen 2021	Multicentre	Nil	Performed	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Prospective	3.6	11
Diehl 2008	Single	Nil	Nil	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Prospective	0	11
He 2020	Single	Nil	Nil	Low	Low	Low	Low	Low	Low	Low	High	High	Low	Prospective	5	9
Huang 2019	Single	Nil	Nil	Low	Low	Low	Low	Low	Low	Low	Low	High	Low	Prospective	4.7	11
Ji 2021	Single	Nil	Nil	Low	High	Low	Low	Low	Low	High	High	High	High	Retrospective study design	30.4	6
Jin 2021	Single	Nil	Nil	Low	Low	Low	Low	Low	Low	Low	High	High	Low	Prospective	0	9
Khakoo 2020	Single	Nil	Nil	Low	Low	Low	Low	Low	High	Low	High	High	High	Prospective	0	7
Lee 2021	Single	Nil	Nil	Low	High	Low	Low	Low	Low	Low	Low	High	Low	Prospective	0	9
LeonArellano 2020	Single	Nil	Nil	Low	High	Low	Low	Low	Low	Low	Low	Low	Low	Prospective	0	10
Levy 2012	Single	Nil	Nil	Low	Low	Low	Low	High	Low	Low	High	Low	Low	Prospective	0	9
Lindforss 2005	Single	Nil	Nil	Low	High	Low	Low	High	Low	Low	High	High	Low	Prospective	0	7
López-Rojo 2020	Single	Nil	Nil	Low	Low	Low	Low	Low	Low	Low	High	High	Low	Prospective	4	9
Mason 2021	Single	Nil	Performed	Low	Low	High	Low	Low	High	Low	High	Low	High	Prospective	18.2	7
Murahashi 2020	Single	Nil	Performed	Low	High	Low	Low	Low	Low	High	High	High	Low	Prospective	0	7
Murray 2018	Single	Performed	Performed	Low	High	Low	Low	Low	High	Low	High	Low	Low	Prospective	23.4	8
Ng 2017	Single	Nil	Nil	Low	High	Low	Low	Low	Low	Low	High	High	Low	Prospective	0	8
Parikh 2021	Single	Nil	Performed	Low	Low	Low	Low	Low	High	Low	Low	Low	Low	Prospective	16.7	10

Reinert 2019	Multicentre	Nil	Performed	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Prospective	16. 7	11
Ryan 2003	Single	Nil	Performed	Low	Low	Low	Low	Low	Low	Low	High	High	Low	Prospective	3.8	10
Schøler 2017	Single	Nil	Nil	Low	Low	Low	Low	Low	Low	Low	High	Low	High	Retrospective design	Not stated	8
Suzuki 2020	Multicentre	Nil	Nil	Low	Low	Low	Low	Low	Low	Low	High	High	Low	Prospective	0	10
Taieb 2021	Low	Nil	Performed	Low	Low	Low	Low	Low	Low	Low	High	Low	Low	Retrospective	0	9
Tanaka 2021	Single	Nil	Nil	Low	Low	Low	Low	Low	Low	Low	High	Low	Low	Prospective	0	10
Tarazona 2019	Single	Nil	Performed	Low	Low	Low	Low	Low	Low	High	Low	Low	Low	Prospective	26.6	10
Tie 2016	Multicentre	Performed	Performed	Low	Low	Low	Low	Low	High	Low	Low	Low	Low	Prospective	8.7	10
Tie 2019 (a)	Low	Nil	Performed	Low	Low	Low	Low	Low	High	Low	Low	Low	Low	Prospective	0	10
Tie 2019 (b)	Multicentre	Performed	Performed	Low	Low	Low	Low	Low	High	Low	Low	High	Low	Prospective	0	9
Tie 2021	Low	Performed	Performed	Low	Low	Low	Low	Low	High	Low	Low	High	Low	Prospective	0	9
Yamada 2016	Single	Nil	Nil	Low	Low	Low	Low	Low	High	Low	High	High	Low	Prospective	0	8
Zhong 2020	Single	Nil	Performed	Low	High	Low	Low	Low	Low	Low	High	High	High	Prospective	0	7
Zhou 2016	Single	Nil	Nil	Low	Low	Low	Low	Low	Low	High	High	Low	High	Prospective	16.7	8
Zhou 2021	Multicentre	Nil	Nil	Low	Low	Low	Low	Low	High	Low	Low	High	Low	Prospective	8.2	9
Zou 2020	Single	Nil	Nil	Low	High	Low	Low	Low	Low	Low	High	Low	High	Prospective	3.4	8

Supplementary Table 4. Quality Assessment. Overall quality assessment score and breakdown of scores within domains for included studies and percentage of sample lost to attrition.

Search strategies

Embase

Database: Embase <1974 to 2021 July 08>

Search Strategy:

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1 ("circulating tumo?r*" adj2 DNA).tw. (5593)

2 ("cell-free" adj2 DNA).tw. (10146)

3 ("circulating free" adj2 DNA).tw. (597)

4 (ctDNA or "ct DNA").tw. (7444)

5 (cfDNA or "cf DNA").tw. (5851)

6 (cftDNA or "cft DNA").tw. (41)

7 plasma DNA.tw. (1779)

8 serum DNA.tw. (656)

9 "circulating nucleic acid*".tw. (668)

10 (KRAS adj2 (mutat* or gene*)).tw. (15519)

11 "kirsten rat sarcoma viral oncogene".tw. (620)

12 "v-Ki-ras*".tw. (338)

13 "Ki-ras".tw. (1407)

14 "K-ras".tw. (9131)

15 (tp53 adj2 (mutat* or gene*)).tw. (15739)

16 "micro-satellite instability-high".tw. (2)

17 "microsatellite instability-high".tw. (802)

18 MSI-H.tw. (2778)

19 "liquid biops*".tw. (7495)

20 circulating tumor DNA/ (5288)

21 microsatellite instability/ (15445)

22 oncogene k ras/ (11316)

23 or/1-22 (83300)

24 (colorectal adj3 (cancer* or neoplasm* or malignan* or carcinoma* or tumo?r* or adenocarcinoma*)).tw. (201238)

25 (colon* adj3 (cancer* or neoplasm* or malignan* or carcinoma* or tumo?r* or adenocarcinoma*)).tw. (129865)

26 (bowel* adj3 (cancer* or neoplasm* or malignan* or carcinoma* or tumo?r* or adenocarcinoma*)).tw. (11500)

27 (rectal* adj3 (cancer* or neoplasm* or malignan* or carcinoma* or tumo?r* or adenocarcinoma*)).tw. (50418)

28 (rectum adj3 (cancer* or neoplasm* or malignan* or carcinoma* or tumo?r* or adenocarcinoma*)).tw. (7573)

29 (sigmoid adj3 (cancer* or neoplasm* or malignan* or carcinoma* or tumo?r* or adenocarcinoma*)).tw. (3575)

30 CRC.tw. (59576)

31 exp colon cancer/ (291109)

32 rectum cancer/ (36860)

33 colon tumor/ (21603)

34 large intestine tumor/ (197)

35 colorectal tumor/ (25343)

36 rectum tumor/ (13637)

37 or/24-36 (439940)

38 colectom*.tw. (21560)

39 proctectom*.tw. (2347)

40 proctocolectom*.tw. (4695)

41 metastectom*.tw. (232)

42 exp abdominal surgery/ (827602)

43 exp intestine surgery/ (222175)

44 surg*.ti. (765246)

45 postsurg*.tw. (26667)

46 postoperat*.tw. (758237)

47 resect*.ti. (118531)

48 su.fs. (2129556)

49 or/38-48 (3290004)

50 23 and 37 and 49 (2794)

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Medline

Database: Ovid MEDLINE(R) ALL <1946 to July 08, 2021>

Search Strategy:

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1 ("circulating tumo?r*" adj2 DNA).tw. (2634)

2 ("cell-free" adj2 DNA).tw. (5594)

3 ("circulating free" adj2 DNA).tw. (282)

4 (ctDNA or "ct DNA").tw. (4031)

5 (cfDNA or "cf DNA").tw. (2532)

6 (cftDNA or "cft DNA").tw. (14)

7 plasma DNA.tw. (1032)

8 serum DNA.tw. (490)

9 "circulating nucleic acid*".tw. (300)

10 (KRAS adj2 (mutat* or gene*)).tw. (7132)

11 "kirsten rat sarcoma viral oncogene".tw. (543)

12 "v-Ki-ras*".tw. (312)

13 "Ki-ras".tw. (1364)

14 "K-ras".tw. (6327)

15 (tp53 adj2 (mutat* or gene*)).tw. (8031)

16 "micro-satellite instability-high".tw. (1)

17 "microsatellite instability-high".tw. (458)

18 MSI-H.tw. (1444)

19 "liquid biops*".tw. (4157)

20 Circulating Tumor DNA/ (1377)

21 or/1-20 (37572)

22 (colorectal adj3 (cancer* or neoplasm* or malignan* or carcinoma* or tumo?r* or adenocarcinoma*)).tw. (134187)

23 (colon* adj3 (cancer* or neoplasm* or malignan* or carcinoma* or tumo?r* or adenocarcinoma*)).tw. (93329)

24 (bowel* adj3 (cancer* or neoplasm* or malignan* or carcinoma* or tumo?r* or adenocarcinoma*)).tw. (7177)

25 (rectal* adj3 (cancer* or neoplasm* or malignan* or carcinoma* or tumo?r* or adenocarcinoma*)).tw. (32836)

26 (rectum adj3 (cancer* or neoplasm* or malignan* or carcinoma* or tumo?r* or adenocarcinoma*)).tw. (6422)

27 (sigmoid adj3 (cancer* or neoplasm* or malignan* or carcinoma* or tumo?r* or adenocarcinoma*)).tw. (2747)

28 CRC.tw. (36057)

29 exp Colorectal Neoplasms/ (211959)

30 or/22-29 (295525)

31 colectom*.tw. (12740)

32 proctectom*.tw. (1350)

33 proctocolectom*.tw. (3136)

34 metastectom*.tw. (88)

35 Colorectal Surgery/ (3719)

36 exp Digestive System Surgical Procedures/ (383491)

37 surg*.tw. (2037096)

38 postsurg*.tw. (20945)

39 postoperat*.tw. (572414)

40 resect*.tw. (374680)

41 su.fs. (2072247)

42 or/31-41 (3472737)

43 21 and 30 and 42 (1310)

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Cochrane

Search Name: ctDNA and colorectal cancer

Date Run: 09/07/2021 20:01:09

Comment: 090721

ID	Search	Hits
#1	((circulating NEXT tumo?r*) NEAR/2 DNA):ti,ab	416
#2	(cell-free NEAR/2 DNA):ti,ab	226
#3	("circulating free" NEAR/2 DNA):ti,ab	28
#4	(ctDNA OR "ct DNA"):ti,ab	454
#5	(cfDNA OR "cf DNA"):ti,ab	164
#6	(cftDNA OR "cft DNA"):ti,ab	2
#7	"plasma DNA":ti,ab	55
#8	"serum DNA":ti,ab	19
#9	("circulating nucleic" NEAR/2 acid*):ti,ab	5
#10	(KRAS NEAR/2 (mutat* OR gene*)):ti,ab	663
#11	"kirsten rat sarcoma viral oncogene":ti,ab	40
#12	v-Ki-ras*:ti,ab	15
#13	Ki-ras:ti,ab	5
#14	K-ras:ti,ab	231
#15	(tp53 NEAR/2 (mutat* OR gene*)):ti,ab	412
#16	"micro-satellite instability-high":ti,ab	0
#17	"microsatellite instability-high":ti,ab	55
#18	MSI-H:ti,ab	99
#19	("liquid" NEAR/2 biops*):ti,ab	128
#20	[mh ^"Circulating Tumor DNA"]	16
#21	{OR #1-#20}	2251
#22	(colorectal NEAR/3 (cancer* OR neoplasm* OR malignan* OR carcinoma* OR tumo?r* OR adenocarcinoma*)):ti,ab	14177
#23	(colon* NEAR/3 (cancer* OR neoplasm* OR malignan* OR carcinoma* OR tumo?r* OR adenocarcinoma*)):ti,ab	4584
#24	(bowel* NEAR/3 (cancer* OR neoplasm* OR malignan* OR carcinoma* OR tumo?r* OR adenocarcinoma*)):ti,ab	629
#25	(rectal* NEAR/3 (cancer* OR neoplasm* OR malignan* OR carcinoma* OR tumo?r* OR adenocarcinoma*)):ti,ab	3737

#26 (rectum NEAR/3 (cancer* OR neoplasm* OR malignan* OR carcinoma* OR tumo?r* OR adenocarcinoma*)):ti,ab 587

#27 (sigmoid NEAR/3 (cancer* OR neoplasm* OR malignan* OR carcinoma* OR tumo?r* OR adenocarcinoma*)):ti,ab 89

#28 CRC:ti,ab 4461

#29 [mh "Colorectal Neoplasms"] 8554

#30 {OR #22-#29} 22347

#31 colectom*:ti,ab 1097

#32 proctectom*:ti,ab 74

#33 proctocolectom*:ti,ab 138

#34 metastectom*:ti,ab 9

#35 [mh ^"Colorectal Surgery"] 202

#36 [mh "Digestive System Surgical Procedures"] 14341

#37 surg*:ti,ab 212530

#38 postsurg*:ti,ab 6549

#39 postoperat*:ti,ab 112538

#40 resect*:ti,ab 26960

#41 MeSH descriptor: [] explode all trees and with qualifier(s): [surgery - SU] 59936

#42 {OR #31-#41} 276555

#43 #21 AND #30 AND #42 196

Quality Assessment form

1. Single or multicentre study

Number of centres patients were recruited from

Single- high risk mulit centre- low risk

2. Patient population

Are the patient population clearly described adequate baseline clinical data collected on cohort

high-no Low-yes

3. Sample size and power calculations

Number of patients recruited, sample size calculations

Low- sample size calculations performed High- not performed

4. Are any co intervention clearly and unambiguously stated

Did patients receive adjuvant chemotherapy following resection, if so was this accounted for and were outcomes presented separately in terms of this.

Did all patients receiving adjuvant chemotherapy receive the same therapy (regimes, duration)

Were the surgical resections performed equivalent between the two groups, were lymph node involvement outcomes comparable, did all patients in the cohort achieve R0 resections

High- no, Low- yes

5. Were different management strategies initiated based on ctDNA results

Were ctDNA levels used to guide treatment decisions

High- yes Low- no

6. ctDNA methodology

was the ctDNA methodology was adequately described

Low- adequately described. High- not well described

7. Cut-off value

Description of cut off for consideration of ctDNA positive/detectable, was this defined beforehand ctDNA status defined prospectively at the time of measurement and not retrospectively after the follow up period

low- clearly defined high- ambiguous

8. Time line consistency

Were there time line consistencies for all ctDNA measurements, how wide was the timing interval over which measurements could be taken

low- set timeframe stated in methods samples collected from sample at same time following surgerry, high- wide range

9. Attrition

Are attrition rates adequately described

high- well described low - poorly described

10. Adjustment

Was multi variate analysis performed, were outcomes presented adjusted for cofounding variables

high- no low- yes

11. Blinding

Were the treating physicians blinded to the ctDNA results when making treatment decisions (ie decisions regarding adjuvant chemotherapy), were assessors blinded to the ctDNA result (positive/negative) when collecting follow up data (OS, PFS)

high- no blinding, low- blinded

12. Clear definition of recurrence

Definition of recurrence- was it confirmed radiologically, was the time at radiological confirmation of recurrence used in calculating PFS.

high- not clearly defined, low- clearly defined, radiologically

13. Selective reporting of results

Outcomes for all groups clearly presented

yes- low, no-high

Data Extraction form

1. Study Details
Study ID
Covidence ID
Title
Author *Surname of first author et al*
Journal published in
Year of publication
Country *Country in which patients were treated*
Journal
Trial ID number or local ethics number
Study centre number *Number of centres data collection took place in*
Additional notes
2. Study Design
Sample size *Total number of patient who completed the study (addressing our study objective), Not including healthy controls or other study groups in the study addressing other research questions*
Attrition *Total attrition number and attrition according to group (ctDNA positive vs negative). Attrition defined as withdrawal from study due to unexpected natural causes not part of disease process or outcomes, eg. lost to follow up, withdrew consent*
Number of patients completed all follow-up
Follow up duration *Median follow up, in months*
Follow up - range *Follow up range in months*
Study timeline □ Prospective □ Retrospective □ Other
Study aims: Primary and secondary study objectives
Inclusion criteria
Exclusion criteria
Post operative monitoring *Method, frequency and duration of post op monitoring after surgery*
Additional notes
3. Patient characteristics
Age *Median age of participant in years to the nearest year* □ Age statistic □ Median □ Mean □ Mode □ Not stated □ Other
Gender *%male to one decimal place*
Histology Histology of cancer primary □ Adenocarcinoma

☐ GIST ☐ NET ☐ Not stated ☐ Other
Cancer stage
Cancer site ☐ Colon ☐ Rectal ☐ Colon and rectal ☐ Metastases ☐ Other
Site- percentage colon *Percentage of cases where the primary site was colon (vs. rectal)*
Cancer side *percentage right sided colon cancer to one decimal place. If not mentioned or not applicable 'not stated'*
Additional notes
Chemotherapy
Neoadjuvant chemotherapy *Proportion of patients in cohort who had chemotherapy prior to surgery (% to one decimal place)*
Neoadjuvant chemotherapy regimes
Adjuvant chemotherapy: percentage of patients *Proportion of patients in cohort who had chemotherapy prior to surgery (% to one decimal place)* Adjuvant chemotherapy regime
Adjuvant chemotherapy duration
Number of cycles
4. ctDNA measurement
Pre surgery levels *Was a liquid biopsy performed prior to surgery* ☐ Yes ☐ No
Timing of pre surgery levels
Number of liquid biopsy post-surgery
Time range over which all liquid biopsies were performed *Time from surgery to timing of last liquid biopsy performed*
Timing of first measurement post-surgery *Time in months after surgery the first liquid biopsy was performed after surgery*
Sample type ☐ Plasma ☐ Serum ☐ Not stated ☐ Other
Method of detection
Gene panel/ target genes
Limit of detection
Cut off level *Cut of level for which measurements were considered 'ctDNA positive', if any above limit of detection*
Additional notes
5. Outcomes
Percentage with detectable ctDNA *Proportion of cohort who were considered ctDNA positive at first liquid biopsy after surgery (% to one decimal place)*

Percentage with detectable ctDNA post-operatively who experienced disease recurrence during the follow-up period *Recurrence defined as radiological recurrence during the follow up period, if more than one liquid biopsy was performed post surgery, patients should be stratified according to the first ctDNA measurement taken after curative surgery or after completion of adjuvant chemotherapy, Percentage to one decimal place*
Percentage with undetectable ctDNA post operatively who experienced disease recurrence during the follow-up period *Recurrence defined as radiological recurrence during the follow up period, if more than one liquid biopsy was performed post surgery, patients should be stratified according to the first ctDNA measurement taken after curative surgery or after completion of adjuvant chemotherapy, percentage to one decimal place*
Mutations detected *Main genes in which mutations were seen*
Percentage with mutations detected *Percentage of patients in whom mutations were detected on ctDNA analysis*
Study conclusions
Multivariate analysis *Were any adjustments for cofounding variables carried out, which variables were adjusted for*
Outcomes
Median PFS ctDNA positive *Median PFS of ctDNA positive patients in months, to nearest month, for all patients*
Median PFS ctDNA negative *Median PFS of ctDNA negative patients in months, to nearest month, for all patients in the cohort*
Hazard ratio *Hazard ratio of PFS for ctDNA positive compared to negative for all patients in the cohort, with 95% confidence intervals and p value.*
Median PFS ctDNA positive (adjuvant chemotherapy) *Median PFS of ctDNA positive patients in months, to nearest month, for patients who received adjuvant chemotherapy*
Median PFS ctDNA negative (adjuvant chemotherapy) *Median PFS of ctDNA negative patients in months, to nearest month, for patients who received adjuvant chemotherapy*
Hazard ratio (adjuvant chemotherapy) *Hazard ratio of PFS for ctDNA positive compared to negative for patients who received adjuvant chemotherapy, with 95% confidence intervals and p value*
Median PFS ctDNA positive (no adjuvant chemotherapy) *Median PFS of ctDNA positive patients in months, to nearest month, for patients who did not receive adjuvant chemotherapy*
Median PFS ctDNA negative (no adjuvant chemotherapy) *Median PFS of ctDNA negative patients in months, to nearest month, for patients who did not receive adjuvant chemotherapy*
Hazard ratio (no adjuvant chemotherapy) *Hazard ratio of PFS for ctDNA positive compared to negative for patients who did not receive adjuvant chemotherapy, with 95% confidence intervals and p value*
Overall survival
Median survival ctDNA positive *In months*
Median survival ctDNA negative *In months*
Hazard ratio *Hazard ratio of OS for ctDNA positive compared to negative patient, with 95% confidence intervals and p value*

References

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