

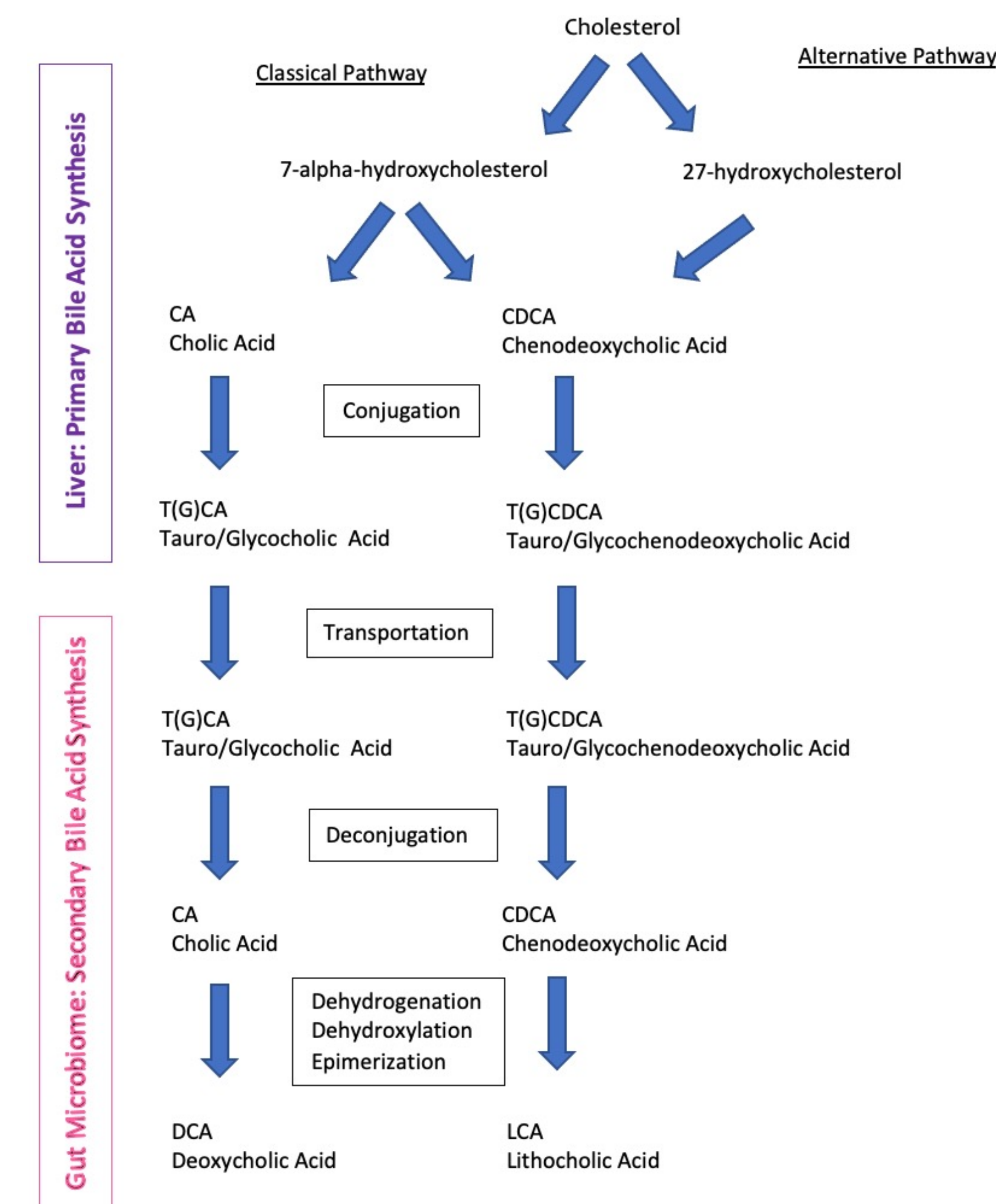
Examining the Impact of Cholecystectomy on Tumor Recurrence in Breast Cancer Patients



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BILE ACID SYNTHESIS & TRANSPORT



BILE ACIDS & BREAST CANCER

- Bile acids regulate many aspects of breast cancer tumor development, progression, and metastases potential.
- Previously published studies have shown that bile acids can have two effects: decreased cancer cell proliferation or promotion of cancer cell growth, and this could be dependent on bile acid concentrations in the serum and tissue exposure.
- Secondary bile acid lithocholic acid (LCA) was shown in vitro to reduce breast cancer cell proliferation and increase the antitumor immune response. Early stage breast cancer patients were found to have decreased levels of LCA in their serum.
- In another study, LCA lowered the infiltration capacity of the primary tumor and reduced the number of metastases.
- Deoxycholic acid (DCA) is found in breast cyst fluid and has co-carcinogenic activity in breast cancer cells.
- Glycophenodeoxycholic Acid (GCDC) increased the growth of cancer cells over a range of 10-300uM, but at higher concentrations was toxic.
- Breast cancer patients have alterations in the circulating levels of bile acids and potentially the exposure of the breast cells to them.
- Cholecystectomy further disrupts bile acid metabolism and circulation and has been shown in mice to increase the bacterial dihydroxylation of bile acids. This leads to a higher proportion of secondary bile acids such as LCA that could either have anti-tumor or co-carcinogenic effects.

METHODS

- Over 90 study subjects were retrospectively identified who were female and diagnosed with invasive ductal carcinoma in 2014.
- Patient demographics, preoperative variables, surgical details, treatment, and clinical outcomes were collected and statistically analyzed.

RESULTS

	Cholecystectomy (n=28)	No Cholecystectomy (n=65)	P-value
Deceased	13 (46%)	15 (23%)	0.0243
Recurrence	10 (36%)	16 (25%)	0.2954
Local	5 (18%)	4 (6%)	
Regional	0 (0%)	2 (3%)	
Distal	5 (18%)	10 (15%)	1.000
Average BMI	32.95	28.53	0.0236
Receptor Status			0.1031
HR+/-Her2-	12 (43%)	36 (55%)	
HR+/-Her2+	8 (29%)	11 (17%)	
HR-/-Her2+	1 (4%)	10 (15%)	
Triple Neg	6 (21%)	9 (14%)	

Patient Characteristic	Value (n=93)
Age	59.7 (± 11.3)
BMI	29.9 (± 7.8)
Stage	
Stage 1	39
Stage 2	35
Stage 3	19
Stage 4	0
Receptor Status	
HR+/-Her2-	48
HR+/-Her2+	19
HR-/-Her2+	11
Triple Negative	15
Neoadjuvant Chemotherapy	10
Surgery	89
Lymph Node Status	
Negative	54
Positive	30
Unknown	9
SLNB	82
Axillary Dissection	20
Radiation	56
Adjuvant Chemotherapy Only	17
Adjuvant Chemotherapy & Endocrine Therapy	17
Adjuvant Endocrine Therapy Only	36
Status	
Deceased	28
Alive	65
Cause of Death	
Breast	12
Other	8
Unknown	8
Smoking Status	
Never	54
Current	13
Former	26
Diabetes Mellitus	25
Statin Use	34
Prior History of Breast Cancer	12
Recurrence	26
Local	9
Regional	2
Distal	15
Cholecystectomy	28

CONCLUSIONS

- Patients with cholecystectomy appear to not have a statistically significant rate of recurrence, but interestingly do have a difference in living status.
- Association between BMI and cholecystectomy in breast cancer patients is likely confounding.
- No statistical significance found in receptor status, but trend is seen.
- The effects of the changes in bile acid modulation following cholecystectomy on breast cancer is still unclear and requires further investigation with larger sample size.
- Cholecystectomy may also alter the microbiota, which is another potential contributing factor of changes in bile acid concentrations.
- Bile acid metabolism could become a target in treatment of breast cancer and recurrence prevention.

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