

KANKER KELENJAR TIROID

OLEH ;
I PUTU ARYA DHARMA

ANATOMI KELENJAR TIROID

- Terletak di leher bag depan bawah, setinggi ring trakea ke-2 sampai ke-3.
- Terdiri dari 2 lobus; kanan dan kiri dan dihubungkan oleh isthmus.
- Berbentuk seperti kupu-kupu, ada juga yg menyebut seperti perisai. (tiroid berasal dari kata Yunani Thyreos yang berarti perisai).
- Masing2 lobus berukuran panjang 3-4 cm dan lebar 2 cm, dg ketebalan beberapa mm.

- Berat saat bayi sekitar 1,5 gr, dan pada dewasa berkisar 15 – 20 gr.
- Dibungkus kapsul jar fibrous tipis, pada sisi posterior melekat erat dg trakea dan laring (ligamentum suspensorium dari Berry) → bergerak saat menelan.
- Vaskularisasi ; A. Tiroidea Superior, A. Tiroidea Inferior, dan A. Tiroidea Ima.
- Sistem Vena ; V. Tiroidea Superior & Media menuju ke V. Jugularis Interna. V. Tiroidea Inferior menuju ke V. Brakisefalika.

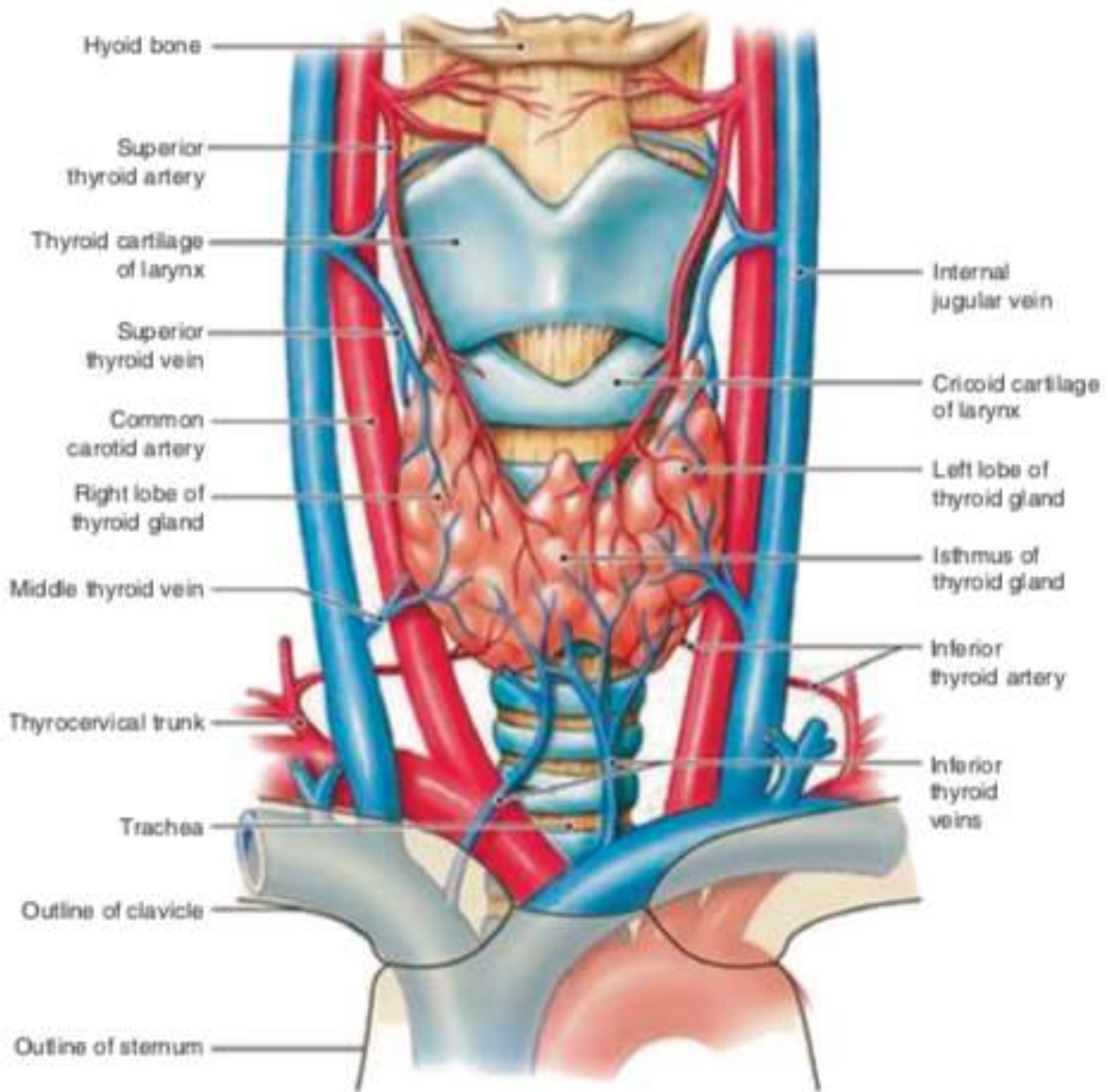


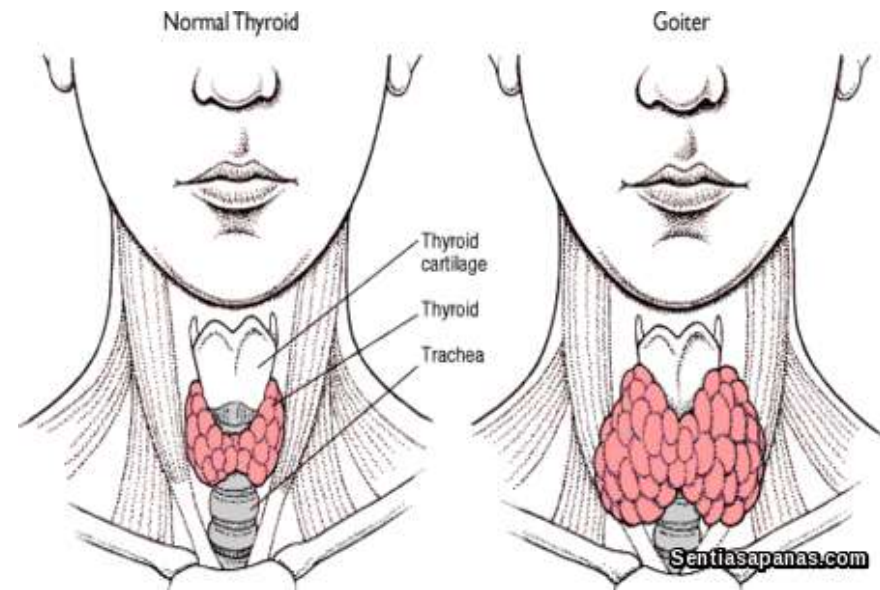
Fig. 1 Anatomy of the thyroid gland. Martini FH, Nath JL, Bartholomew EF. *Fundamentals of Anatomy and Physiology*, 10th ed. ©2015. Reprinted by permission of Pearson Education, Inc., New York, New York

FISIOLOGIS KELENJAR TIROID

- Menghasilkan hormon Tiroksin.
- Mempunyai peranan penting dalam pengaturan laju metabolisme tubuh, penghasil energi, dan mengatur fungsi organ, seperti jantung dan otak.
- Mekanisme produksi hormon diatur oleh Thyroid Stimulating Hormone (TSH), yang diproduksi oleh kelenjar Hipofise Anterior. Juga oleh sistem auto regulasi di dalam kelenjar Tiroid sendiri.

STRUMA (GOITER)

- Adalah Tumor (pembesaran) kelenjar Tiroid.
- Dianggap membesar bila ukuran lebih dari 2x ukuran normal.
- Dibedakan ; Diffusa dan Nodusa (Uni/Multi)
- Hipertiroid, Eutiroid, dan Hipotiroid.



PATOFISIOLOGI STRUMA

- **Hiperplasia dan Hipertrofi** ; akibat kebutuhan meningkat, seperti pertumbuhan, pubertas, dan hamil.
- **Infeksi/Inflamasi** ;
 1. Tiroiditis Akut
 2. Tiroiditis Sub-akut (de Quervain)
 3. Tiroiditis Kronis (Hashimoto's ds, Riedel's struma)
- **Neoplasma** ; jinak atau ganas.

KANKER KELENJAR TIROID

- Merupakan keganasan endokrin yang tersering, dengan insiden di dunia 3,1%.
- Di Indonesia menempati urutan ke 11 dari kanker tersering, dengan insiden 3,3% per tahun.
- 90% merupakan kanker yang berdiferensiasi baik.
- Prognosis baik pada kanker yang berdiferensiasi baik ; survival 5 th mencapai 100%. Tapi pada kanker anaplastik, survival 5 th hanya berkisar 5%.

Klasifikasi Histopatologis

TABLE

17.1

Pathologic Classification of Thyroid Malignancies

| Subtype | Variants | Incidence |
|------------------------------|----------------------|-----------|
| Well Differentiated | | |
| Papillary (80%) | Conventional | 65–85% |
| | Follicular | 15–20% |
| | Tall cell | 5–10% |
| | Solid | 1–3% |
| | Diffuse sclerosing | 1–2% |
| | Columnar | <1% |
| Follicular (10%) | Hürthle cell variant | |
| Hürthle Cell (5%) | | |
| Poorly Differentiated | Insular | |
| Medullary (5%) | | |
| Anaplastic (1–5%) | | |
| Other | Lymphoma | |
| | Metastatic | |

Incidence is representative for each variant of a particular subtype.

WHO classification of tumours of the thyroid gland (2017)

| | | | |
|--|---------|--|--------|
| Follicular adenoma | 8330/0 | Paraganglioma and mesenchymal/stromal tumours | |
| Hyalinizing trabecular tumour | 8336/1* | Paraganglioma | 8693/3 |
| Other encapsulated follicular-patterned thyroid tumours | | Peripheral nerve sheath tumours (PNSTs) | |
| Follicular tumour of uncertain malignant potential | 8335/1* | Schwannoma | 9560/0 |
| Well-differentiated tumour of uncertain malignant potential | 8348/1* | Malignant PNST | 9540/3 |
| Noninvasive follicular thyroid neoplasm with papillary-like nuclear features | 8349/1* | Benign vascular tumours | |
| Papillary thyroid carcinoma (PTC) | | Haemangioma | 9120/0 |
| Papillary carcinoma | 8260/3 | Cavernous haemangioma | 9121/0 |
| Follicular variant of PTC | 8340/3 | Lymphangioma | 9170/0 |
| Encapsulated variant of PTC | 8343/3 | Angiosarcoma | 9120/3 |
| Papillary microcarcinoma | 8341/3 | Smooth muscle tumours | |
| Columnar cell variant of PTC | 8344/3 | Leiomyoma | 8890/0 |
| Oncocytic variant of PTC | 8342/3 | Leiomyosarcoma | 8890/3 |
| Follicular thyroid carcinoma (FTC), NOS | 8330/3 | Solitary fibrous tumour | 8815/1 |
| FTC, minimally invasive | 8335/3 | Hematolymphoid tumours | |
| FTC, encapsulated angioinvasive | 8339/3 | Langerhans cell histiocytosis | 9751/3 |
| FTC, widely invasive | 8330/3 | Rosai-Dorfman disease | |
| Hürthle (oncocytic) cell tumours | | Follicular dendritic cell sarcoma | 9758/3 |
| Hürthle cell adenoma | 8290/0 | Primary thyroid lymphoma | |
| Hürthle cell carcinoma | 8290/3 | Germ cell tumours | |
| Poorly differentiated thyroid carcinoma | 8337/3 | Benign teratoma | 9080/0 |
| Anaplastic thyroid carcinoma | 8020/3 | Immature teratoma | 9080/1 |
| Squamous cell carcinoma | 8070/3 | Malignant teratoma | 9080/3 |
| Medullary thyroid carcinoma | 8345/3 | Secondary tumours | |
| Mixed medullary and follicular thyroid carcinoma | 8346/3 | | |
| Mucoepidermoid carcinoma | 8430/3 | | |
| Sclerosing mucoepidermoid carcinoma with eosinophilia | 8430/3 | | |
| Mucinous carcinoma | 8480/3 | | |
| Ectopic thymoma | 8580/3 | | |
| Spindle epithelial tumour with thymus-like differentiation | 8588/3 | | |
| Intrathyroid thymic carcinoma | 8589/3 | | |

The first four digits indicate the specific histological term; the fifth digit after the slash (/) is the behavior code, including /0 for benign tumours, /1 for unspecified, borderline, or uncertain behavior, /2 for carcinoma in situ and grade III intraepithelial neoplasia, and /3 for malignant tumours

* These new codes were approved by the IARC/WHO Committee for ICD-O

- **Mc Kenzie**, membedakan Kanker Tiroid menjadi 4, untuk memudahkan penatalaksanaan, yaitu :
 1. Karsinoma Papiler
 2. Karsinoma Folikuler
 3. Karsinoma Medulare
 4. Karsinoma Anaplastik

PAPILLARY

- ✦ Most common type of thyroid cancer
- ✦ Represents 75 - 85% of thyroid cases

75-85%



FOLLICULAR

- ✦ Well differentiated tumor
- ✦ Accounts for 15% of thyroid cases

15%



MEDULLARY

- ✦ Originates from the parafollicular cells
- ✦ Represents 3 % of the thyroid cases

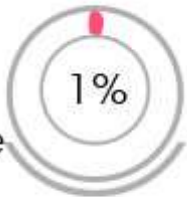
3%



ANAPLASTIC

- ✦ Most aggressive form of thyroid cancer
- ✦ Accounts for only 1% of the thyroid cases

1%





Carcinoma of Thyroid



Type (%) age spread Prognosis

| | | | | |
|--------------------------------|--------------|---|--|---|
| Papillary | 60-70 | young adults 20-40 (<45y) | Lymphatic , to local nodes | Excellent |
| Follicular | 20-25 | Young-middle 40-50 (>45) | Blood stream, especially to bone | Good with radio-iodine therapy. |
| Anaplastic | 10-15 | Elderly | Aggressive local extension | Very poor |
| Medullary (C-cells) | 5-10 | Usually elderly, but familial cases occur | Local, lymphatic, blood stream | Variable. More aggressive in familial cases |

KLASIFIKASI KLINIS TNM AJCC edisi 8-2018

TNM definitions (AJCC 8e)

for papillary, follicular, poorly differentiated, Hürthle cell, medullary, and anaplastic thyroid carcinomas

| | |
|------|--|
| TX | Primary tumor cannot be assessed |
| T0 | No evidence of primary tumor |
| T1 | Tumor ≤ 2 cm in greatest dimension limited to the thyroid |
| T1a | Tumor ≤ 1 cm in greatest dimension limited to the thyroid |
| T1b | Tumor > 1 cm but ≤ 2 cm in greatest dimension limited to the thyroid |
| T2 | Tumor > 2 cm but ≤ 4 cm in greatest dimension limited to the thyroid |
| T3* | Tumor > 4 cm limited to the thyroid or gross extrathyroidal extension invading only strap muscles |
| T3a* | Tumor > 4 cm limited to the thyroid |
| T3b* | Gross extrathyroidal extension invading only strap muscles (sternohyoid) from a tumor of any size |
| T4 | Includes gross extrathyroidal extension into major neck structures |
| T4a | Gross extrathyroidal extension invading subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve from a tumor of any size |
| T4b | Gross extrathyroidal extension invading prevertebral fascia or encasing carotid artery or mediastinal vessels from a tumor of any size |

| | |
|------|--|
| NX | Regional lymph nodes cannot be assessed |
| N0 | No evidence of regional lymph nodes metastasis |
| N0a* | One or more cytologic or histologically confirmed benign lymph node |
| N0b* | No radiologic or clinical evidence of locoregional lymph node metastasis |
| N1* | Metastasis to regional nodes |
| N1a* | Metastasis to level VI or VII (pretracheal, paratracheal, or prelaryngeal/Delphian, or upper mediastinal) lymph nodes; this can be unilateral or bilateral disease |
| N1b* | Metastasis to unilateral, bilateral, or contralateral lateral neck lymph nodes (levels I, II, III, IV, or V) or retropharyngeal lymph nodes |

M0 No distant metastasis

M1 Distant metastasis

* all categories may be subdivided as solitary tumor (s) and multifocal tumor (m) – the largest tumor determines the classification

PENGELOMPOKAN STADIUM KLINIS

Staging flowchart for differentiated thyroid cancer (AJCC 8e)

| Age at diagnosis | M category | Gross ETE | Structures involved | Tumor size | N category | Stage |
|------------------|---|-----------|-------------------------|---------------|------------|------------|
| <55 years | M0 | yes or no | | any | any | I |
| | M1 | yes or no | | any | any | II |
| ≥ 55 years | M0 | no | | ≤ 4 cm (T1-2) | N0/Nx | I |
| | | | | > 4 cm (T3a) | N1a/N1b | II |
| | | | | | any | any |
| | | yes | only strap muscle (T3b) | any | any | II |
| | s/cutaneous, larynx, trachea, esophagus, RL nerve (T4a) | | any | any | III | |
| | prevertebral fascia, encasing major vessels (T4b) | | any | any | IVA | |
| | M1 | yes or no | any or none | any | any | IVB |

Medullary Thyroid Cancer

- **Stage** **TNM**
- I T1, N0, M0
- II T2–3, N0, M0
- III T1–3, N1a, M0
- IVA T4a, N0–1a, M0; T1–4a, N1b, M0
- IVB T4b, any N, M0
- IVC Any T, any N, M1

Anaplastic Cancer

- **Stage** **TNM**
- IVA T4a, Any N, M0
- IVB T4b, Any N, M0
- IVC Any T, Any M, M1

PROSEDUR DIAGNOSTIK

ANAMNESIS :

- Riwayat radiasi
- Pertumbuhan cepat
- Suara serak
- Gejala obstruksi jalan nafas ; nafas bunyi, nafas berat
- Gangguan menelan
- Riwayat keluarga : MEN
- Tetap membesar dg Th/ Tiroksin
- Umur < 20 th atau > 50 th
- Riwayat kel genetik ; Sindroma Werner, Cowden's Ds, dan Familial Adenomatous Polyposis

PROSEDUR DIAGNOSTIK

PEMERIKSAAN FISIK :

- Nodul padat dan keras
- Terfiksasi dg jaringan sekitar
- Pembesaran KGB regional
- Penyempitan jalan nafas
- Paralisis pita suara
- Horner's Syndrome ; miosis, ptosis, anhidrosis, enophthalmus
- Tanda metastase jauh ; tulang, paru, jar. lunak

PEMERIKSAAN KELENJAR TIROID



PROSEDUR DIAGNOSTIK

PEMERIKSAAN PENUNJANG ;

1. PEMERIKSAAN LABORATORIUM

- Kadar FT4 dan TSHs
- Tiroglobulin (untuk kanker berdiferensiasi baik; papiler dan folikuler), hanya utk follow up pasca terapi bukan utk diagnostik
- Kadar Kalsitonin utk karsinoma meduler

PEMERIKSAAN PENUNJANG ;

2. PEMERIKSAAN RADIOLOGI

- Foto Toraks ; menilai metastase
- Foto polos cervical AP/Lat ; mikrokalsifikasi, trakea
- Esofagogram (tidak rutin)
- Bone scan ; bila curiga metastase ke tulang
- CT Scan, MRI, atau PET Scan (tidak rutin)

3. PEMERIKSAAN USG

- Mampu deteksi nodul uk 2-3 mm
- Solid atau kistik
- Jumlah, letak, ukuran, pembesaran KGB, pengarah biopsi jarum halus, respon terapi supresi.
- Tanda ganas ; vascularisasi intranodul, mikrokalsifikasi sentral, batas ireguler, servikal adenopati

PEMERIKSAAN PENUNJANG ;

4. PEMERIKSAAN SIDIK TIROID

- Nodul dingin (cold ndule)
- Nodul hangat (warm nodule)
- Nodul panas (hot nodule)
- Tidak mutlak

5. PEMERIKSAAN BAJAH (FNAB)

- Akurasi ; 50 – 97%
- Bagus untuk jenis kanker papilare, medulare dan anaplastik
- Jenis Folikuler tidak bisa membedakan adenoma dg adeno ca

Table 3 Bethesda system for reporting thyroid cytopathology

| Diagnostic category | Type | Malignancy risk (%) | Management | Frequency reported (%) |
|----------------------------------|--|---------------------|----------------------------------|------------------------|
| Nondiagnostic/ unsatisfactory | Pure cyst poor sample quality | 1–4 | Repeat US-FNA | <10 |
| Benign | Lymphocytic thyroiditis Adenomatoid nodule Colloid nodule Granulomatous thyroiditis | 0–3 | Clinical follow-up | 54–74 |
| Indeterminate | Low risk (AUS/FLUS) | 5–15 | Repeat FNA | 10–20 |
| | High risk (FN/SFN) | 15–30 | Lobectomy | |
| Suspicious for malignancy | Suspicious for | | | |
| | PTC | | | 2.5–5.0 |
| | MTC | 60–75 | Total thyroidectomy or lobectomy | |
| | Metastatic carcinoma | | | |
| | Lymphoma | | | |
| Malignant | PTC | | | |
| | MTC | | | |
| | Poorly differentiated carcinoma | 95–99 | Total thyroidectomy | 4.0–5.4 |
| | Anaplastic | | | |
| | Lymphoma | | | |
| | Metastatic carcinoma | | | |

AUS atypia of undetermined significance, *FLUS* follicular lesion of undetermined significance, *FN* follicular neoplasm, *SFN* suspicious for follicular neoplasm, *PTC* papillary thyroid carcinoma, *MTC* medullary thyroid carcinoma [32, 63, 111–113]

PEMERIKSAAN PENUNJANG ;

6. POTONG BEKU (FROZEN SECTION)

- Dilakukan saat operasi, untuk menentukan tindakan definitif.
- Ketepatan ; 87 – 91%

7. HISTOPATOLOGI

- Merupakan pemeriksaan definitif atau Baku Emas.
- Dilakukan sesudah tindakan operasi.

PEMERIKSAAN PENUNJANG ;

8. IMUNOSITOKIMIA (ISK) ATAU IMUNOHISTOKIMIA

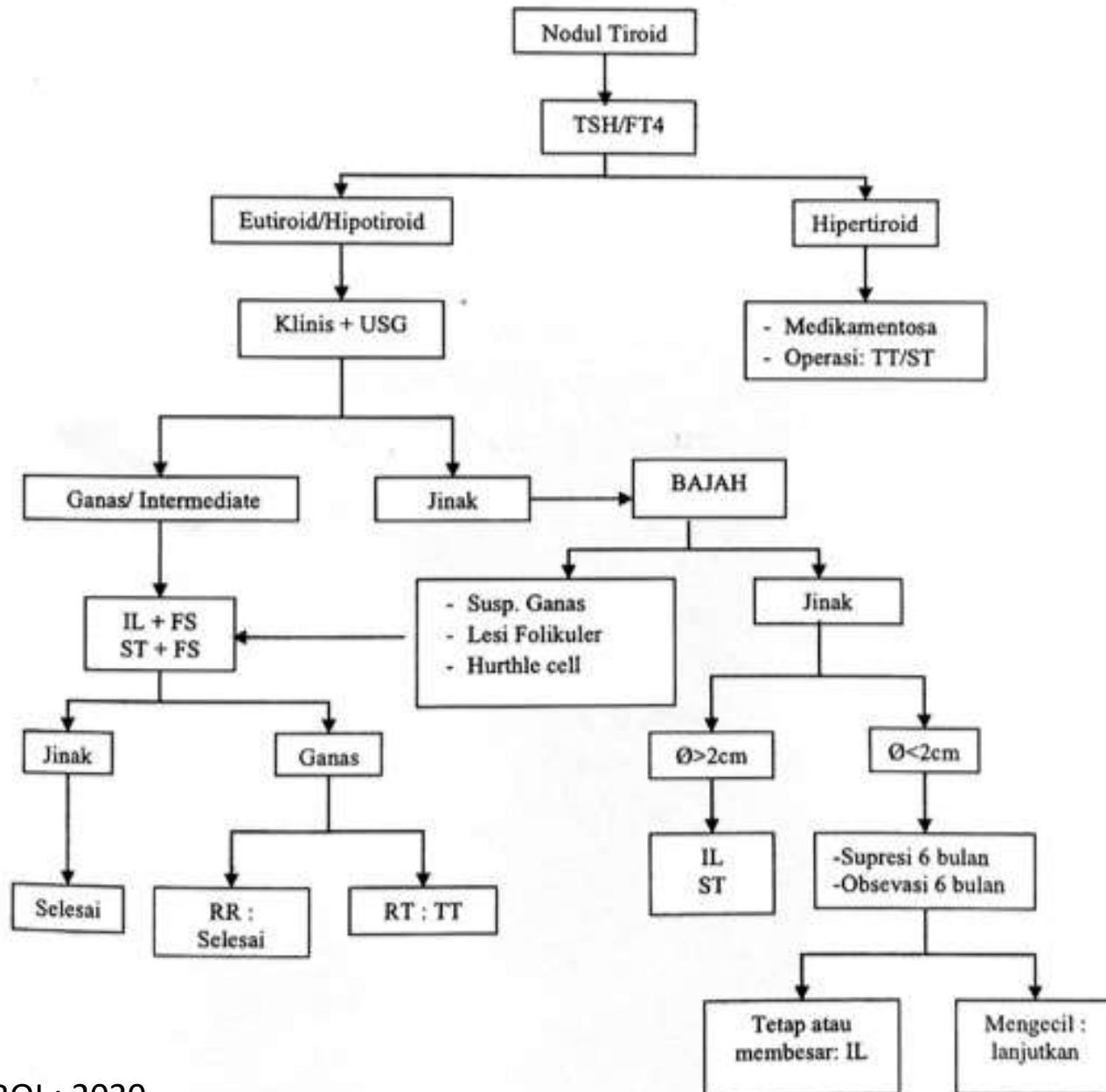
- Pada BAJAH dg hasil Indeterminate ; AUS, FLUS
- Mutasi BRAF dan/atau RAS, rearrangement RET/PTC atau PAX8/PPAR.
- Membedakan jinak atau ganas.
- Prediksi agresivitas kanker dan prognosis.
- Tidak rutin.

PENATALAKSANAAN NODUL TIROID

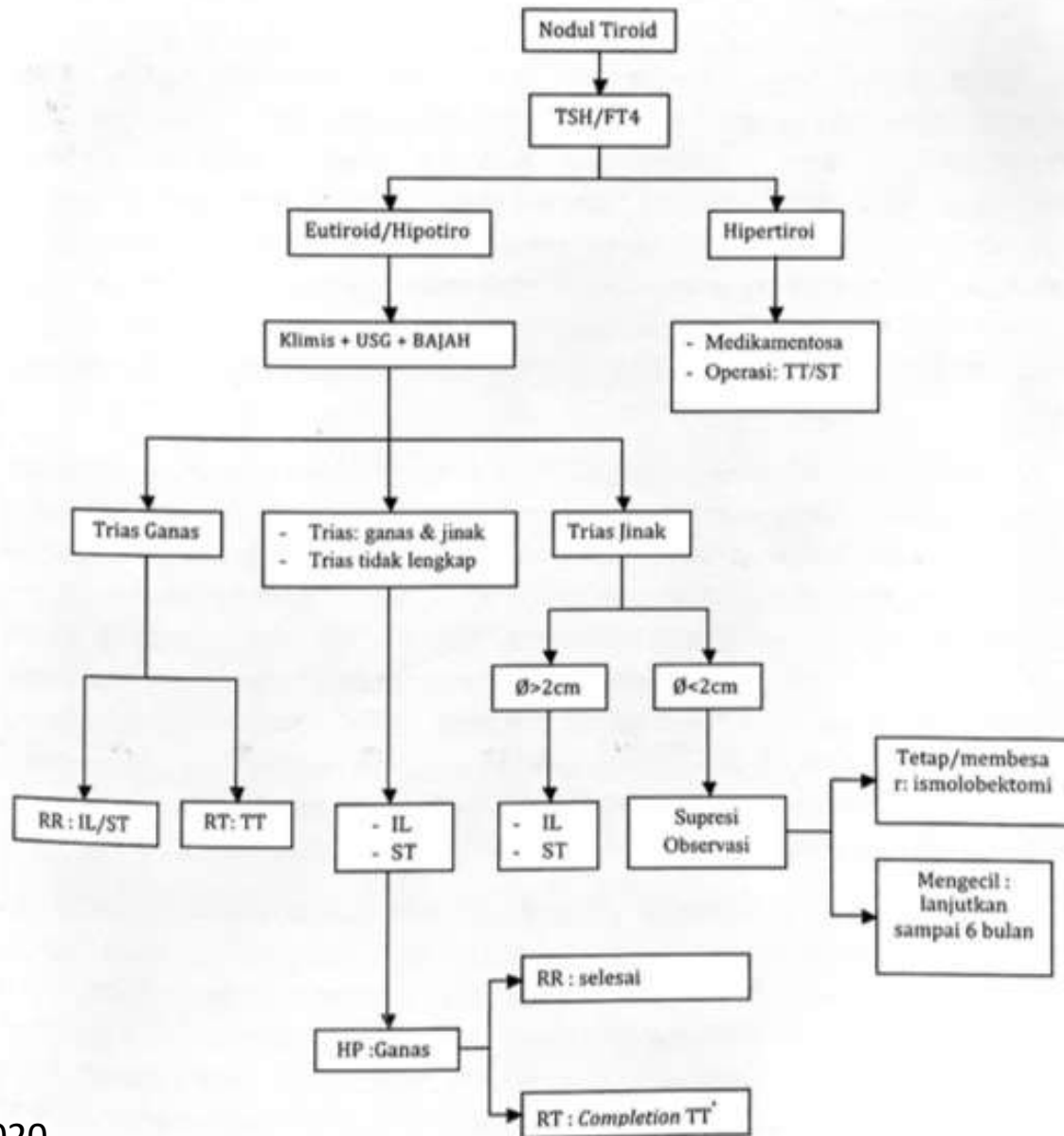
Ada 3 jenis algoritma penatalaksanaan nodul tiroid tergantung dari fasilitas RS dan DPJP, yaitu ;

- a. Algoritma dengan Potong Beku (FZ)
- b. Algoritma dengan Trias Diagnostik (klinis, USG, BAJAH)
- c. Algoritma dengan Trias Diagnostik dan Sidik Tiroid

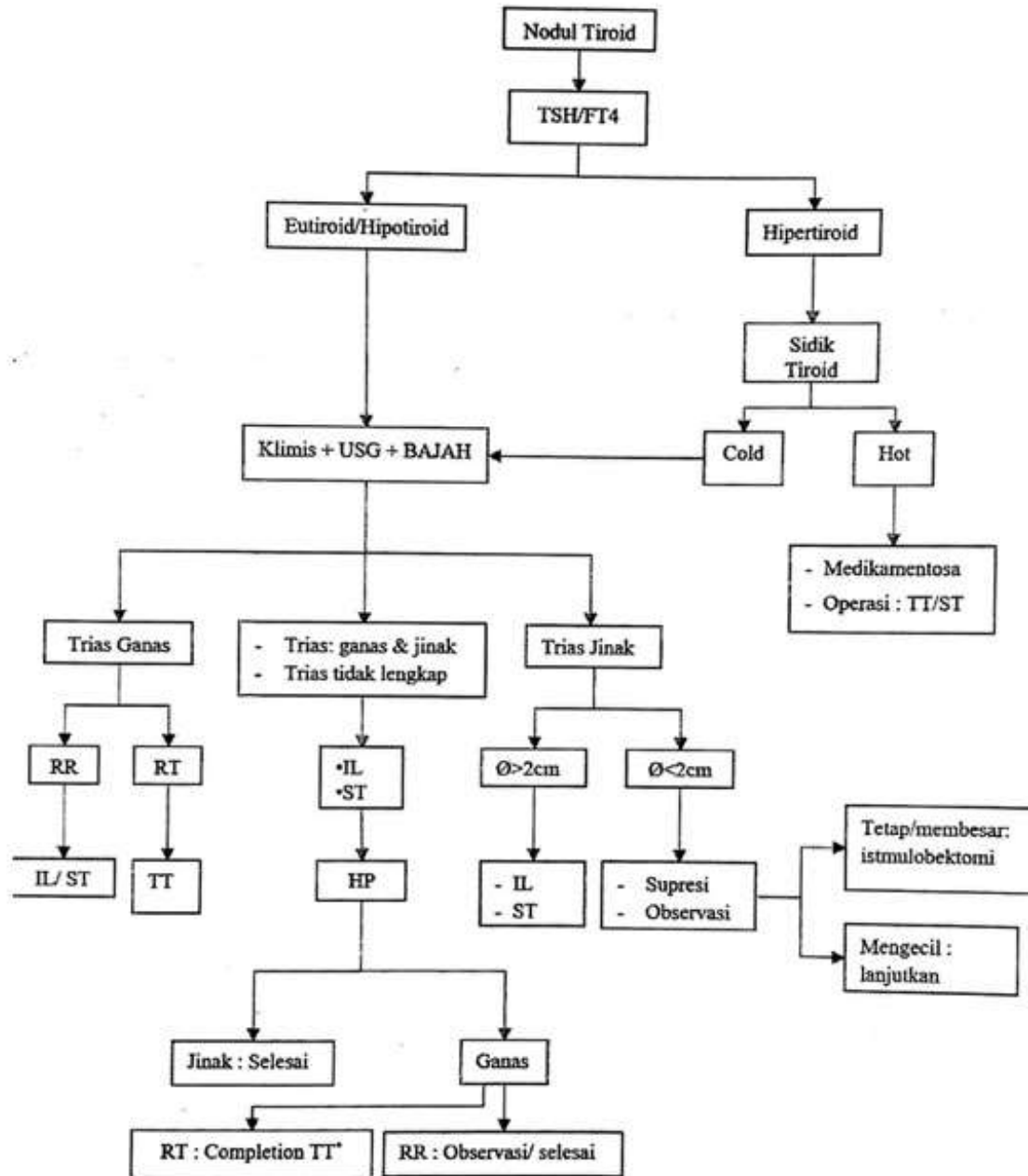
PENATALAKSANAAN DENGAN POTONG BEKU (FROZEN SECTION)



PENATALAKSANAAN DENGAN TRIAS DIAGNOSTIK



PENATALAKSANAAN DENGAN TRIAS DIAGNOSTIK DAN SIDIK TIROID



KLASIFIKASI PROGNOSIS

Prognostic Factors

| Mayo | Lahey | Mayo | Karolinska | MSKCC |
|--------------|-------------------|---|--------------------------|----------------------------|
| AGES | AMES | MACIS | DAMES | GAMES |
| Age Grade | Age Metastases | Metastases Age Completeness Of resection | DNA Age Metastases | Grade Age Metastases |
| Extension | Extension | Invasion | Extension | Extension |
| Size | Size | Size | Size | Size |



Prognostic risk classification for patients based on AMES or AGES

| | Risk | |
|------------|--|---|
| parameter | LOW | HIGH |
| age | <40 | >40 |
| gender | female | male |
| extent | No local extension, intrathyroidal, no capsular invasion | Capsular invasion, extrathyroidal extension |
| metastasis | none | Regional or distant |
| size | <2 cm | >4 cm |
| grade | Well differentiated | Poorly differentiated |

SURVIVAL (20 TAHUN)

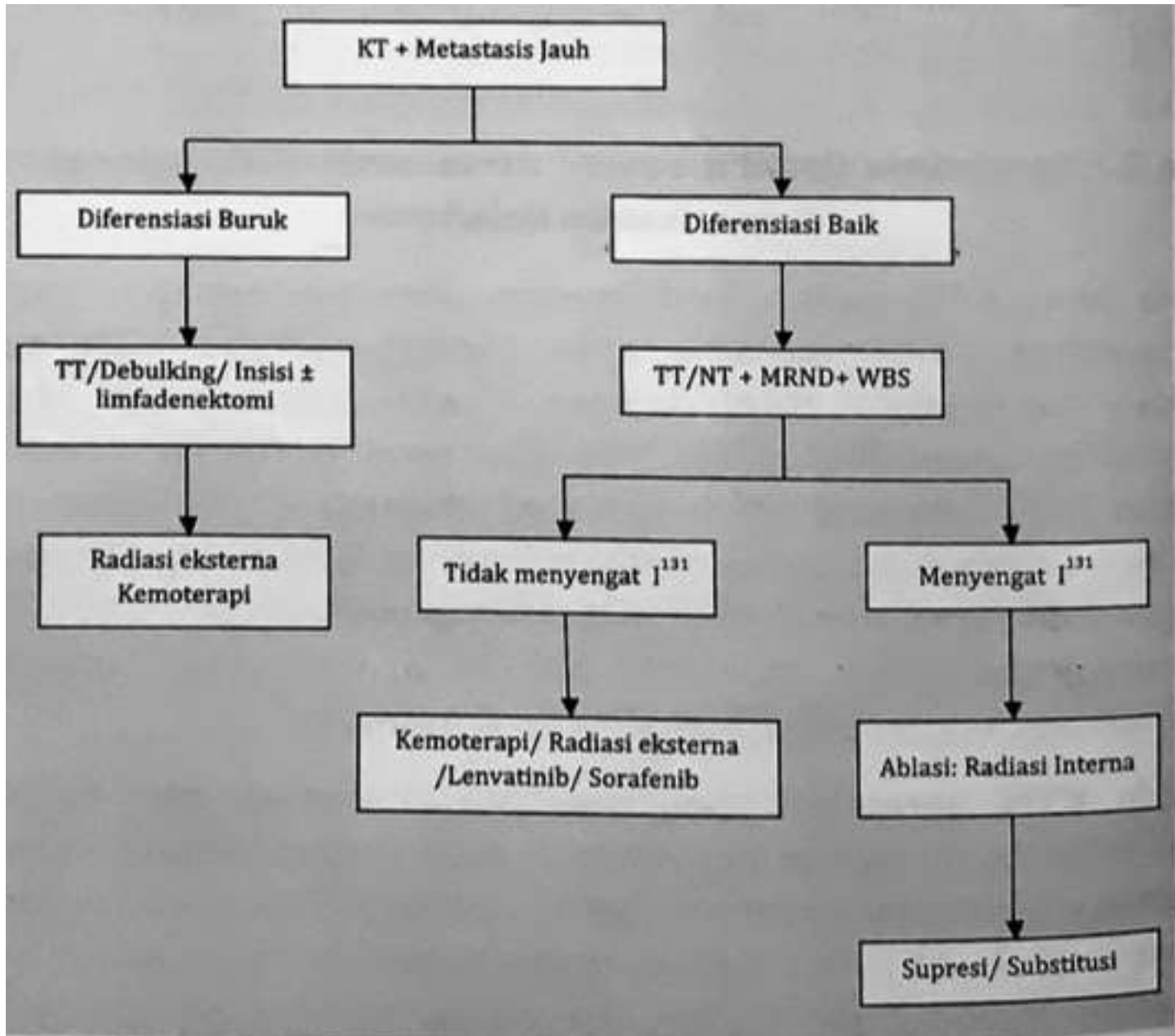
RISIKO RENDAH = 99%

RISIKO TINGGI = 61%

KANKER TIROID DENGAN METASTASE JAUH

- Bedakan apakah berdiferensiasi baik atau buruk.
- Tentukan apakah masih operable atau tidak.
- Untuk kanker yang berdiferensiasi baik, dibedakan apakah menyengat (uptake) terhadap I^{131} atau tidak.
- Kemoterapi ; Doxorubicin, dosis 50-60mg/m², dan Cisplatin 40mg/m², siklus 21 hari.
- Terapi target ; Lenvatinib, Sorafenib.
- Metastase tulang ; biphosponat
- Metastasektomi

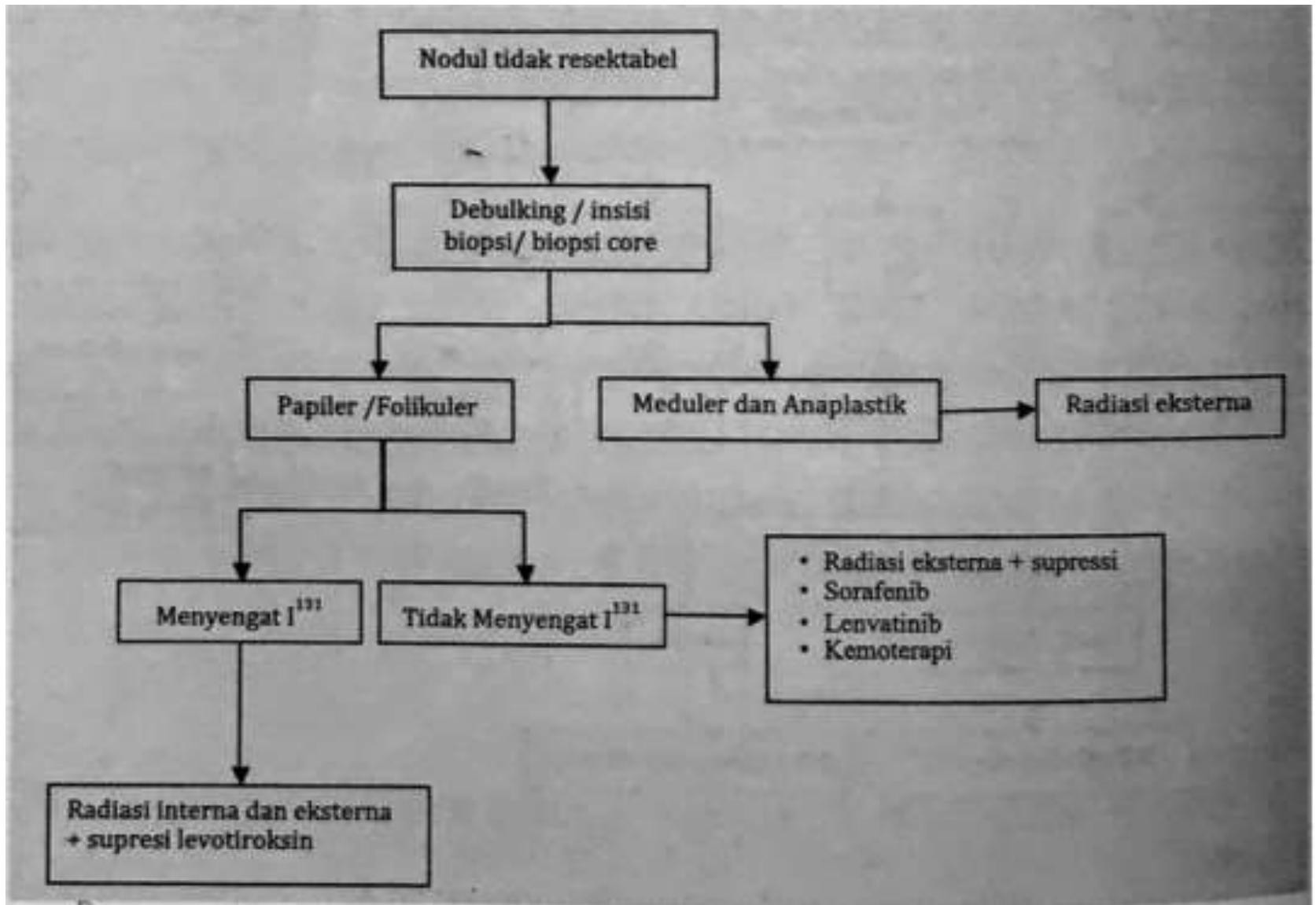
KANKER TIROID DENGAN METASTASE JAUH



NODUL TIROID YANG TIDAK RESEKTABEL

- Minimal dilakukan biopsi untuk menentukan tipe histopatologis.
- Kalau memungkinkan dilakukan operasi “Debulking”.
- Pilihan terapi ; Radiasi (interna/eksterna), Kemoterapi, dan Terapi target.

NODUL TIROID TIDAK RESEKTABEL



FOLLOW UP

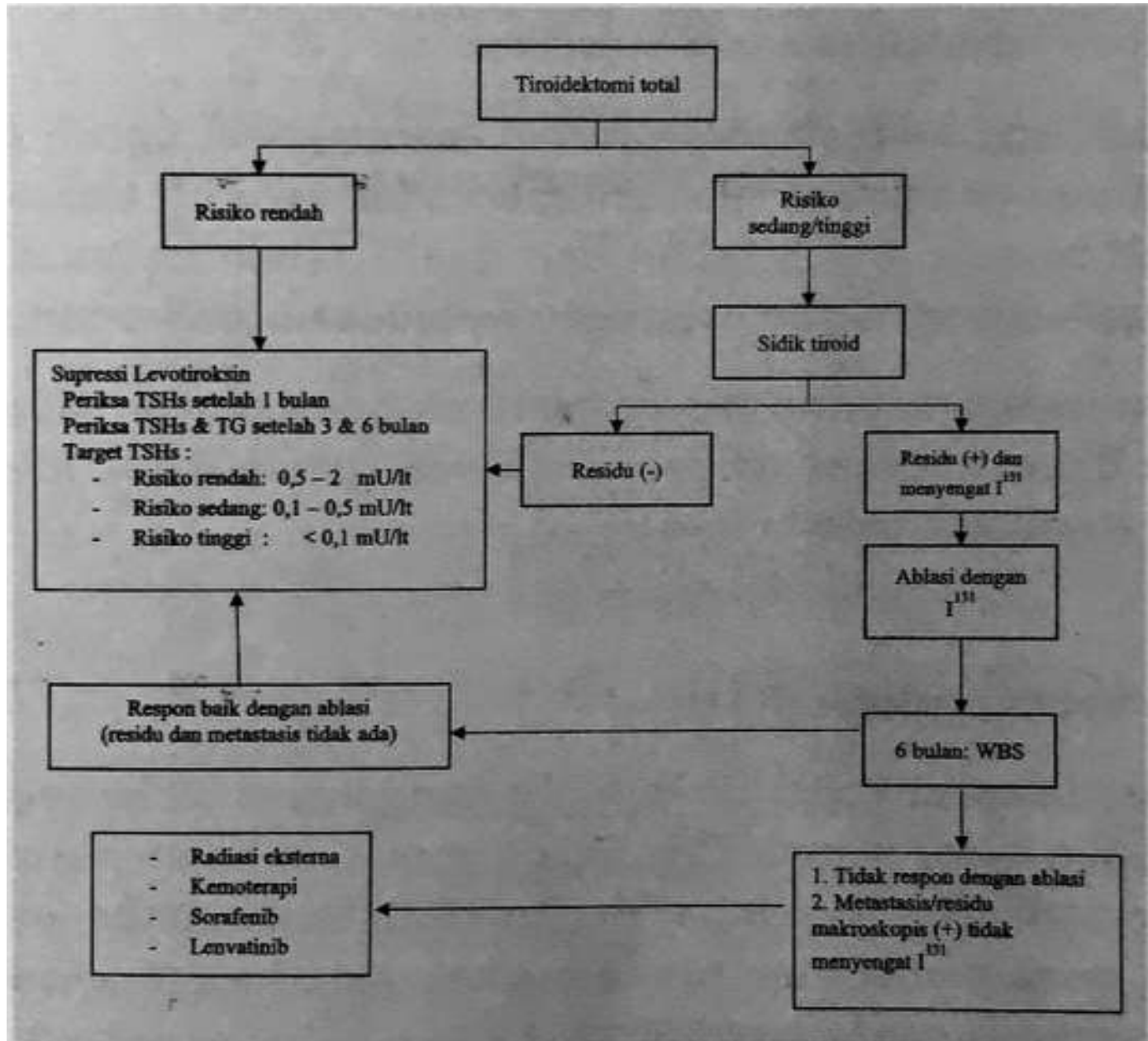
FOLLOW UP KARSINOMA TIROID BERDIFERENSIASI BAIK

- Karsinoma Papiler dg resiko rendah ; th/ supresi Levotiroksin, target TSHs: 0,5-2 mU/l
- Pada resiko sedang-tinggi : 4 minggu pasca TT dilakukan sidik tiroid.
 - Bila (+) ; dilakukan ablasi dg I^{131} , dilanjutkan th/ supresi Levotiroksin dg target TSHs ; 0,1-0,3 mU/l.
 - Bila (-) ; th/ substitusi Levotiroksin, dosis 2,1 mcg/KG BB.

FOLLOW UP KARSINOMA TIROID BERDIFERENSIASI BAIK

- 6 bulan dg th/ substitusi; WBS (stop th 3-4 minggu)
 - Bila metastase jauh (+) dan uptake radioaktif ; radiasi interna + th/ supresi.
 - Bila metastase jauh (-) ; th/ substitusi. WBS diulang @ tahun (2-3 th), selanjutnya @ 3 th.
- Pemeriksaan kadar Tiroglobulin sebagai penanda tumor mendeteksi kemungkinan adanya residif.

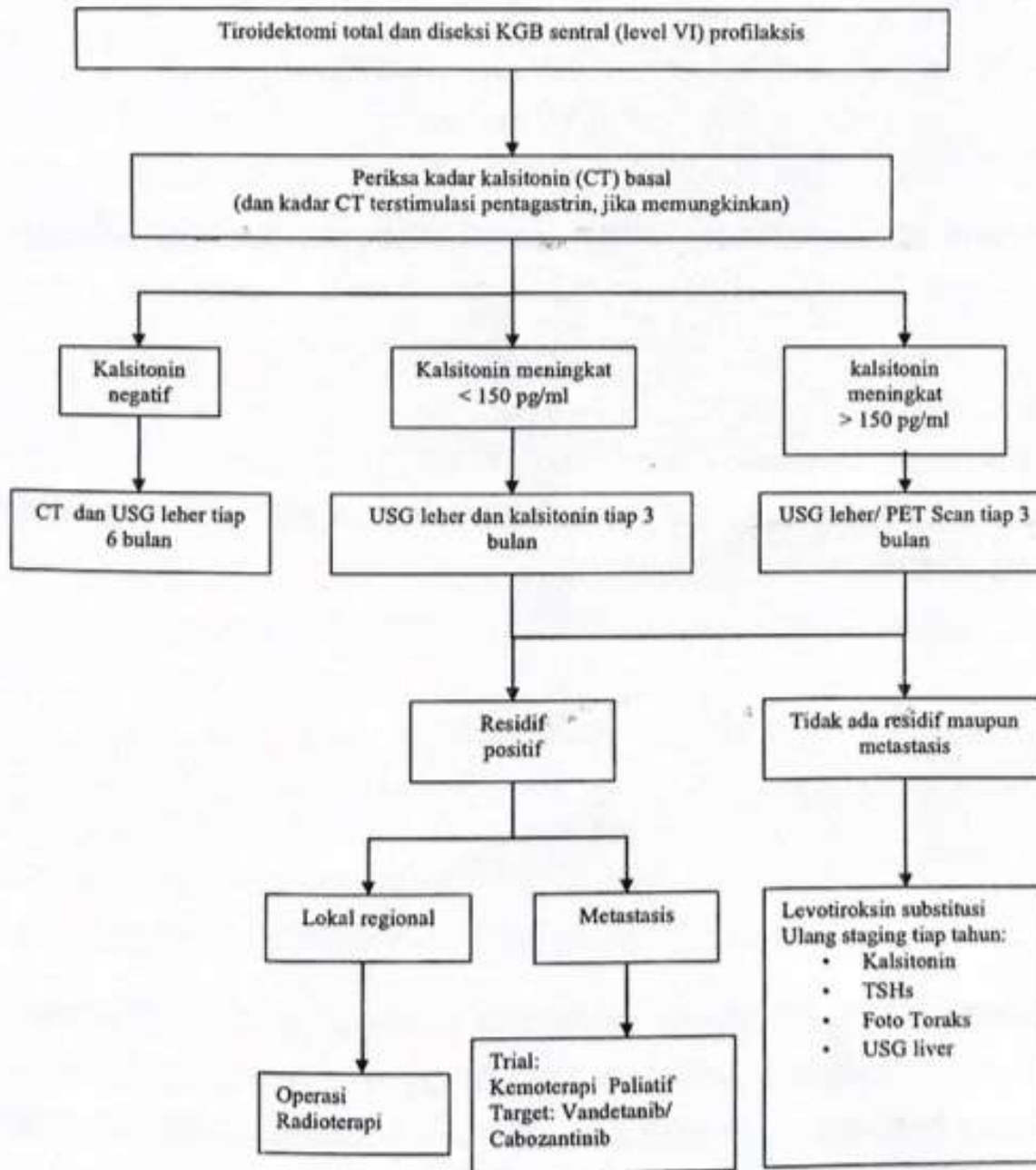
FOLLOW UP KANKER TIROID BERDIFERENSIASI BAIK



FOLLOW UP KANKER TIROID MEDULER

- Pasca operasi diberikan th/ substitusi dg Levotiroksin sampai kadar TSHs normal.
- 2-3 bulan pasca operasi ; periksa ulang TSHs, kadar kalsitonin basal atau kalsitonin terstimuli pentagastrin.
- Residif lokal regional ; operasi + radioterapi.
- Metastase jauh ; kemoterapi (paliatif) dan terapi target (Vandetinib, Cabozantinib).
- Bila residif (-) ; evaluasi rutin setiap 1 th.

FOLLOW UP KANKER TIROID MEDULER



FOLLOW UP KANKER TIROID ANAPLASTIK

- Prognosa buruk, Median Overall Survival hanya 4,9 bulan & harapan hidup 1 th hanya 20%.
- Faktor prediktor utk survival ;
 1. Ukuran tumor (< 5 cm; baik)
 2. Komplet reseksi.
 3. Metastase jauh.
- Follow up rutin setiap 1-3 bl utk 1 th pertama, selanjutnya setiap 4-6 bl (pem fisik, USG leher, CT scan leher & toraks, MRI, PET Scan).

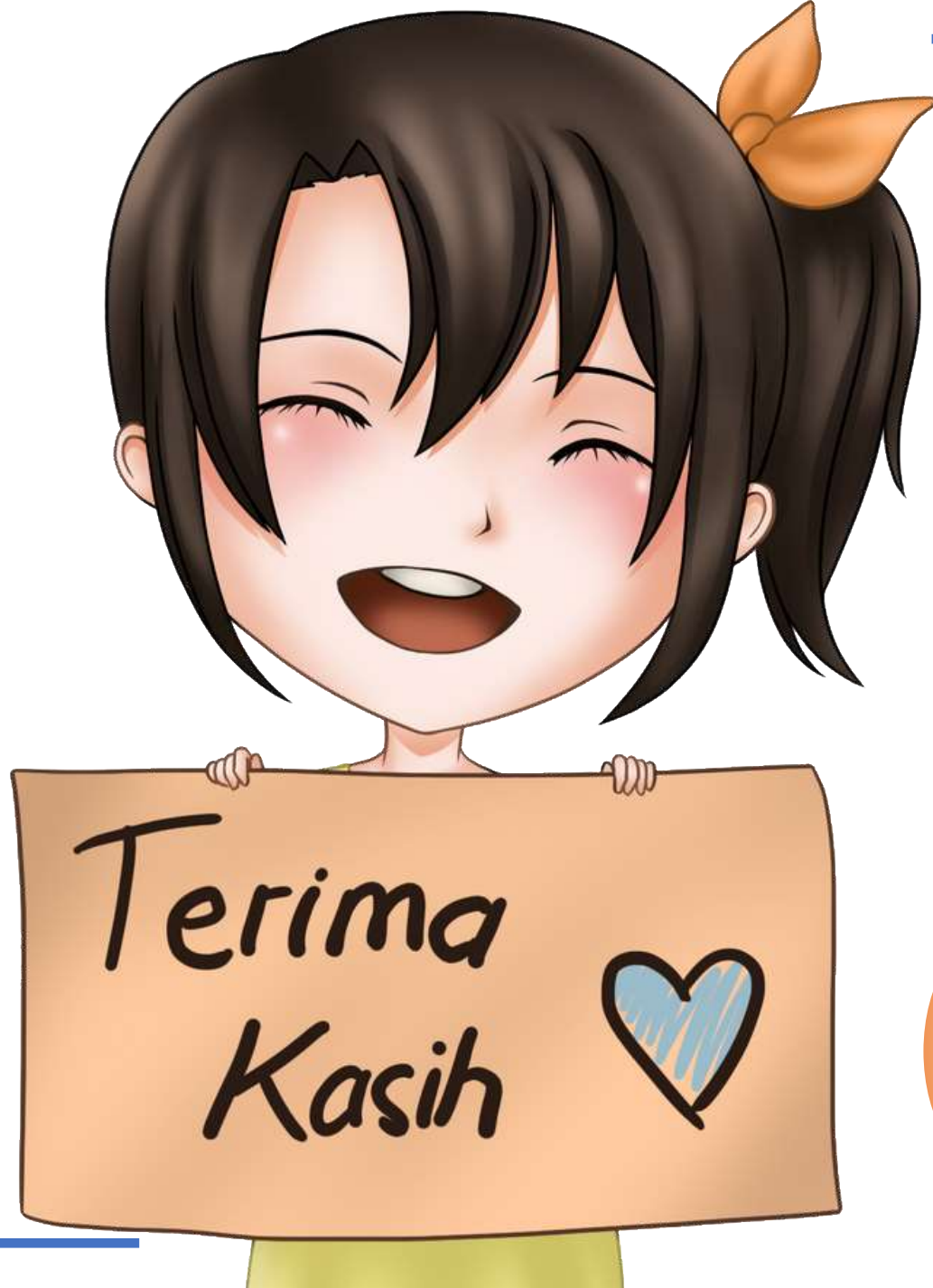
PROGNOSIS

Prognosis depends mainly on the type of cancer and [cancer stage](#).

| Thyroid cancer type | 5-year survival | | | | | 10-year survival |
|---------------------|-------------------|----------|-----------|----------|---------|------------------|
| | Stage I | Stage II | Stage III | Stage IV | Overall | Overall |
| Papillary | 100% | 100% | 93% | 51% | 96% | 93% |
| Follicular | 100% | 100% | 71% | 50% | 91% | 85% |
| Medullary | 100% | 98% | 81% | 28% | 85% | 75% |
| Anaplastic | (always stage IV) | | | 7% | 7% | (no data) |

KESIMPULAN

- Kanker tiroid merupakan keganasan endokrin tersering dg insiden di Indonesia sebesar 3,3% pertahun.
- 90% merupakan kanker berdiferensiasi baik.
- Penatalaksanaan tergantung dari tipe histopatologis, stadium klinis, resiko prognostik, serta ketersediaan fasilitas, sarana diagnostik dan terapi.
- Prognosis relatif baik pada yang berdiferensiasi baik, namun prognosis buruk pada tipe anaplastik.



Semoga
bermanfaat