

Recent Advances in the Diagnosis and Management of Primary Headache Disorders

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Introduction

Headache is a costly public health problem and causes tremendous loss of productivity. Primary headache disorders mainly consist of migraine, tension headache, cluster headache and an entity known as chronic daily headache. The overall prevalence of migraine and tension headache in Hong Kong (for individuals aged above 15) is estimated to be 4.7% and 26.9% respectively. In primary level school children the prevalence of headache is lower at 2.8% (tension-type headache 1.2%, migraine 0.5%, probable migraine 0.7% and unclassified 0.5%) and an increasing prevalence figure is evident towards adolescence. A better diagnosis followed by more targeted therapeutic approach is essential in providing adequate pain relief which is often sub-optimal in this group of patients.

Migraine

Most patients with severe or refractory headache have migraine, transformed migraine or chronic daily headache and history taking is the cornerstone of making the proper diagnosis. However, investigations have to be taken to exclude possible secondary causes when appropriate (Table 1). The most helpful clinical pointer to a migrainous phenomenon in contrast to tension-type headache is nausea, which carries a sensitivity of 82% and specificity of 96%. Photophobia, phonophobia, unilateral throbbing headache and worsening by physical

activity are moderately predictive of migraine. It is not uncommon for migraine to coexist with tension headache or transform into a different pattern known as chronic daily headache (see below). Under these circumstances conventional prophylactic medications e.g. beta-blockers, tricyclic antidepressants, calcium antagonists, and valproate fail to control the headaches in about one third of cases. Very often the picture is complicated by analgesic abuse and withdrawal rebound headache necessitating referral to specialist tertiary center. Comorbid conditions such as anxiety-depression, psychological distress and personality disorder would also require psychiatric intervention.

The most effective drugs for termination of an acute attack of migraine are the triptans or 5HT₁ agonists e.g. sumatriptan, zolmitriptan, naratriptan, rizatriptan. Major side effects of this group are usually self-limited and comprise chest pressure, flushing, paresthesia and drowsiness. Sumatriptan is the first generation prototype with a full range of delivery options available, ranging from subcutaneous, oral to intranasal preparations. Among the newer oral triptans with faster onset of action, 10 mg rizatriptan, 80 mg eletriptan and 12.5 mg almotriptan are comparable in efficacy and generally well tolerated. It is possible that some patients may respond to one triptan but not the other. For those who have contraindications to triptans e.g. ischemic heart disease, complicated migraine, coronary spasm, uncontrolled hypertension, they may be given droperidol 2.5 mg intramuscularly and a success rate of about 70-80% is reported. The American approach favors pethidine (meperidine) injection in intractable cases but chronic administration may give rise to addiction. A recent trial shows that the efficacy of droperidol is comparable to intramuscular pethidine given at a dose of 2.5 mg/kg.

The association between migraine and epilepsy and proposed common pathogenetic mechanism has led to advocate in using antiepileptic drugs (AED) in preventing

Table 1. Some important organic causes which may mimic migraine

Intracranial structural disease e.g. brain tumor
ENT and dental e.g. sinusitis, temporomandibular joint disorders
Head injury e.g. post-traumatic syndrome
Cerebrovascular diseases
Cervical spine e.g. facet joint syndromes
Drug related or withdrawal syndromes e.g. cyclosporin
Severe hypertension e.g. pheochromocytoma
Connective tissue diseases e.g. SLE

migraine. The classical drug being studied in the 1990s is divalproex. When given at a dose of 400 mg twice daily for 2 months, divalproex is shown to reduce migraine attack rate by 50%. In clinical practice it is moderately effective and possible untoward reactions include obesity, dyspepsia, tremor, somnolence and alopecia. Topiramate, gabapentin and levetiracetam also appear to be promising new AED in reducing migraine frequency by 50-70% but larger trials are necessary to confirm their efficacy.

Perhaps the most interesting development in headache prevention is the use of pericranial botulinum toxin A (BTX-A) injections. Pain relief is often observed in patients with cervical dystonia, myofascial pain syndromes and rectal fissure shortly following botulinum injections. When this new treatment is extended to cosmetic usage for reducing forehead wrinkles, a significant proportion of subjects with migraine also reported improvement of their headache. The direct muscle relaxant effect may explain its efficacy in tension headache in which myogenic pain is believed to be important. However, there is scepticism about extending this treatment to migrainers because the mechanism of action of BTX does not fit well into the pathogenesis of migraine. In a recent double blind, vehicle controlled study of 123 subjects with moderately severe migraine, pericranial injection of 25 units of BTX-A was shown to be safe and effective in reducing attack frequency, severity and associated vomiting. The preliminary success reported in this study would suggest suppression of pain pathways by BTX through some unknown effect on the sensory system.

Cluster Headache

Cluster headache is relatively uncommon compared to migraine or tension headache but its distinctive characteristics permit diagnosis to be made clinically. A longstanding history of disabling periodic unilateral

headache (usually retro-orbital) in an otherwise healthy man is classical. Autonomic features such as lacrimation, sweating, conjunctival injection, nasal blockade are unique and frequently present. About 50% of these attacks occur with a predictable time (e.g. awakening at 2 am with a distressing pain lasting for 2 hours). Misdiagnosis as migraine, trigeminal neuralgia or psychogenic is not uncommon resulting in inappropriate therapy in about 50% of cases.

Of the acute abortive treatments available, subcutaneous sumatriptan has been shown to be effective within 15 minutes after injection. Alternatives include intranasal sumatriptan, inhalation of oxygen (7L/min) for 15 minutes, oral high dose zolmitriptan and intravenous ergotamine. Prophylaxis is the mainstay of treatment in those with chronic cluster, high relapse rate or long bout of attack. High dose verapamil, lithium carbonate, and methylsergide are proven effective treatments. In particular, short course steroids may provide rapid relief while the preventive medication is being introduced. There is always some concern about the risk of inducing avascular osteonecrosis and the shortest course of prednisolone associated with this problem is a 30-day course. Hence, a tapering course of steroid for 14 to 21 days is a justifiable effective option.

Although the pathophysiology and clinical features of cluster headache and trigeminal neuralgia are distinct (Table 2), both appear to involve central trigeminal-thalamic pathways as shown by PET studies. In addition, satisfactory control of chronic cluster headache is often obtained following radiofrequency lesioning of the trigeminal ganglion. Taken together, these observations suggest that AED may be effective for cluster headache prevention. Reports of studies in small number of patients indicate that valproate, topiramate and gabapentin are useful for cluster headache prophylaxis with better side effect profiles.

Table 2. Comparison between cluster headache and trigeminal neuralgia

	Cluster headache	Trigeminal neuralgia
Age of onset	before 25	45-70
Sex predominance	male	female
Duration of attack	15-180 min	seconds
Distribution of pain	periorbital	maxillary/mandibular
Autonomic features	frequent	absent
Precipitating factors	alcohol, smoking	trigger points

(List of reference available on request)

Chronic Daily Headaches

Chronic daily headaches can be arbitrarily defined as more than 15 headaches (each lasting >4 hours) per month without evidence of an organic disorder. Four major subcategories are recognized: transformed migraine, chronic tension type headache, new daily persistent headache and hemicrania continua. The majority of this group consists of migraine plus tension headache with or without analgesic abuse. Preventive drug treatment failure is common and a multidisciplinary approach is often required with input from neurologist, anesthetist and psychiatrist. New treatment modalities e.g. pericranial botulinum toxin A injections, antispasticity agent (e.g. tizanidine), and

new AED may offer hope for those who are refractory to conventional therapy.

Again it has to be emphasized that important secondary causes need to be excluded before implementing various forms of new therapy. For instance, obstructive sleep apnoea (OSA) is a potential cause of chronic daily headache and successful treatment with CPAP, weight reduction or corrective surgery will simply eliminate the daily headache. Given that OSA is common in our population with an estimated prevalence of 4.1% among middle aged men, a history of habitual snoring, excessive day-time sleepiness or essential hypertension would warrant a sleep study.

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The Mammogram and Mammographic Report

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Mammography is a major technique in the evaluation of the breast. It is also widely practiced in the screening of breast cancer. Interpretation of mammogram is difficult because of the wide 'normal' appearances. Appearances in mammogram not only differ for different women but also in the same woman at different ages. An understanding of the anatomy, and pathology of the breast will be helpful in the interpretation of mammogram.

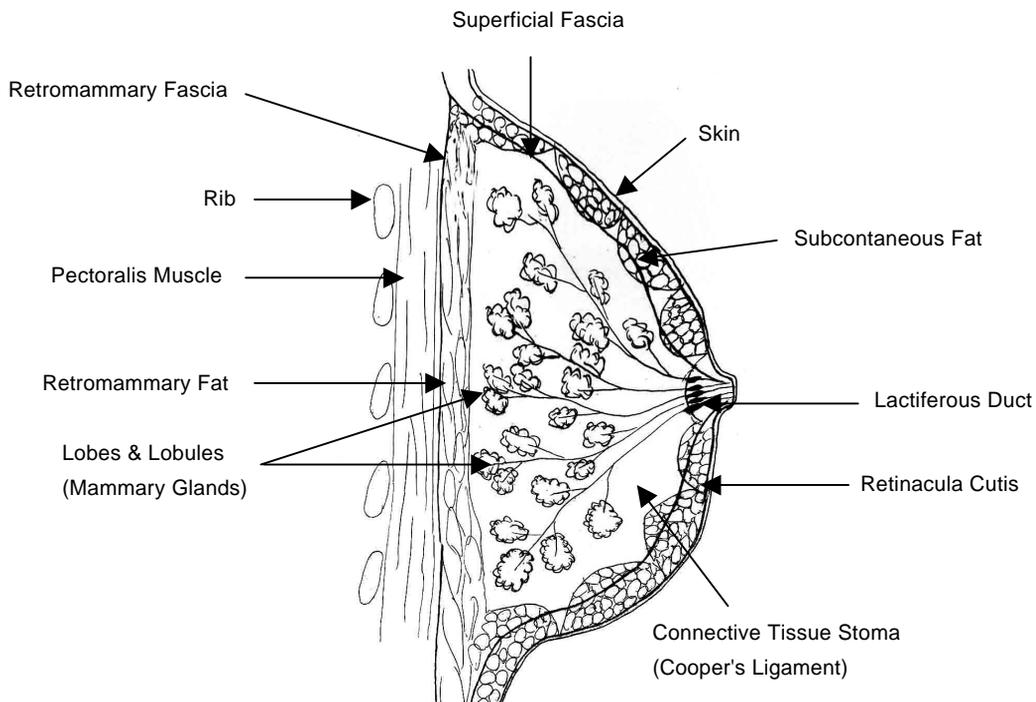
Anatomy of the Breast

The functional element of the breast is the glandular tissue, grouping into 8-20 lobules. Each lobule drains into a lactiferous duct that leads to the nipple. Beneath the nipple, these lactiferous ducts dilate to form the lactiferous sinuses. The ducts ramify into subsegmental structures and finally form the terminal ducts that end into lobules (Terminal duct lobular unit).

The glandular and ductal elements of the breast are supported by connective tissue elements called the Cooper's ligaments. These send slips to attach to the skin as the retinacula cutis.

Inside the breast is a varying amount of fatty tissue. Fat is present in connective and glandular tissue septae. They are also present immediately beneath the skin as subcutaneous fat and behind the glandular tissue as retromammary fat.

The breast is enveloped by two fascial structures. The superficial fascia lies just beneath the skin. The deep fascia (retromammary fascia) lies behind the retromammary space and is immediately anterior to the fascia that covers the pectoralis major muscle.



Relationship Between Breast Disease and Anatomy

- The terminal duct lobular unit (TDLU) consists of the extralobular terminal duct and the lobule. It is a basic histopathologic unit of the breast and give rises to most of the benign and malignant diseases of the breast. These include ductal carcinoma, lobular carcinoma, fibroadenoma and most components of fibrocystic disease: cysts, apocrine metaplasia, adenosis and epitheliosis.
- Diseases of the main duct and its branches include benign and malignant papillary tumours and duct ectasia. They mainly present clinically with nipple discharges and are best evaluated by ductogram.

Mammographic Views

There are two standard views in mammography: medial lateral oblique view (MLO view) and cranial caudal view (CC view). In the medial lateral oblique view the breast is compressed along the oblique fibres of the pectoralis major muscle (30° to 60° to horizontal). It is the single view that images most of the breast tissue. The axillary tail of the breast is also included in this view. The cranial caudal view images the breast in a cranial caudal position. Additional views sometimes are needed for further evaluation of the breast. These include medial lateral view and compression/magnification view.

The normal appearances of MLO view and CC view are shown below (Figure 1).

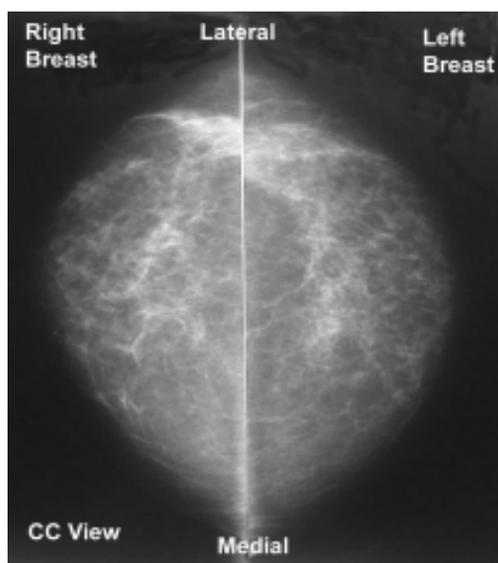


Figure 1. The standard mammographic views: The images of both breasts are usually displayed together for ease of comparison. In the MLO view, the pectoralis major muscle is constantly imaged and appears as a triangular density at the upper part of the radiograph. Sometimes, lymphnodes are seen in the axilla, overlapping the pectoralis major muscle.

The density of the breast depends on the amount of fatty tissue and the amount of glandular and connective tissue in the breast. Terminal duct lobular units appear as 1 mm small nodular densities on mammography. Ductal systems, fibrous strands and vessels appear as linear densities. Whereas vessels can run in any directions in the breast, ducts run towards the nipple. The more the fatty tissue, the lesser dense will be the breast. In general, the older the woman, the more fatty replacement occurs and the lesser dense the breast will become. In contrast, the density of the breast is increased in nulliparous women, women with estrogen replacement and in women with weight loss. In women with dense breasts, pathology is more easily hidden and overlooked. Ultrasound would be useful either as a primary technique (for young women) or as a complimentary exam in such situations.

The Mammographic Report

The report usually starts by a description of the general breast tissue type which range from entirely fatty to extremely dense. This description gives an indication of the sensitivity of the mammogram. The denser the breast tissue, the lower will be the sensitivity. It is recognized that 10-15% of symptomatic carcinoma are not detected by mammography. The report would also include comparison to previous mammogram if any.

The main content of the report describes the significant findings in mammogram. The American College of

Radiologists has developed the BI-RADS (Breast Imaging Reporting and Data System). This standardizes the terminology used in mammography and enhances the communications in mammography interpretation. Readers interested in the BI-RADS can visit the following website: http://www.acr.org/department/stand_accred/birads/contents.html

Detection and analysis of mass lesions and calcifications are most important in the interpretation of mammogram. One should also look for other associated findings such as skin thickening, nipple retraction, abnormal adenopathy (enlarged nodes without fatty hilae) asymmetric density and architectural distortion.

Mass Lesions

A mass by definition is a three dimensional object. It should be seen in more than one view. Lesion seen only in our view should be described as density.

The BI-RADS lexicon describes a mass according to its shape (round, oval, lobular or irregular), density (high, equal, low or fat-containing) and margin (circumscribed, microlobulated, obscured, indistinct and speculated). By far, the most important feature is the margin. Masses with spiculated margins (Figure 2) are likely to be

malignant, while those with indistinct margins (Figure 3) are suspicious. Notice that obscured margin is different from indistinct margin. Obscured margin means that the margin is hidden by overlying breast tissue. They should be further evaluated by compression / magnification views to eliminate the overlying tissue. Circumscribed masses (Figure 4) are usually benign, the most common pathology being cyst and fibroadenoma.

Another useful sign is fat-containing (radiolucent) density. Fat-containing densities are benign and includes lipoma (Figure 5), harmartoma (fibroadenolipoma) oil cyst and galactocele.

Calcifications

The BI-RADS lexicon describes calcifications according to their morphology and distribution. Calcifications with benign morphology include: coarse (Figure 6), large rod like (Figure 7), round (Figure 8), lucent-centered, eggshell (Figure 9) , sedimentation (Figure 10), suture (Figure 11), dystrophic and punctuate. Those with intermediate concern include amorphous calcifications. Calcifications with suspicious morphologies include pleomorphic (granular) calcifications (Figure 12) and fine/linear/branching (casting) calcifications (Figure 13). Illustration examples are shown below:

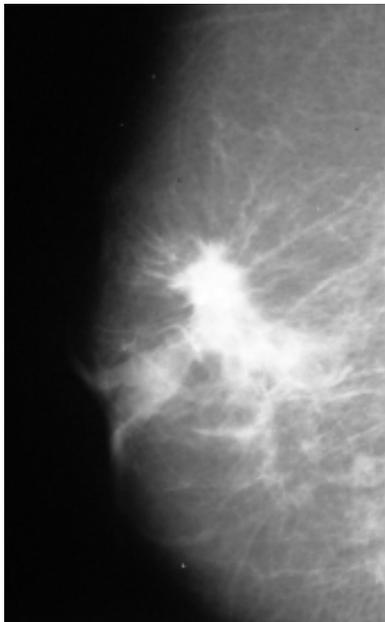


Figure 2. Spiculated Mass. This is an infiltrating carcinoma. The likelihood of spiculated masses being malignancy is about 75 %. Notice the associated nipple retraction.

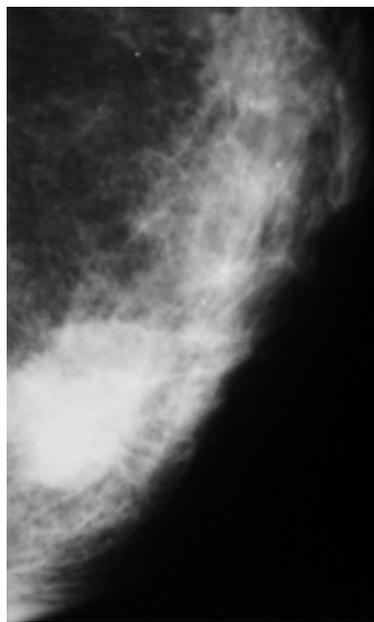


Figure 3. Indistinct Mass. This is an infiltrating carcinoma. The likelihood of indistinct masses being malignancy ranges from 5% to 35% in various reports.

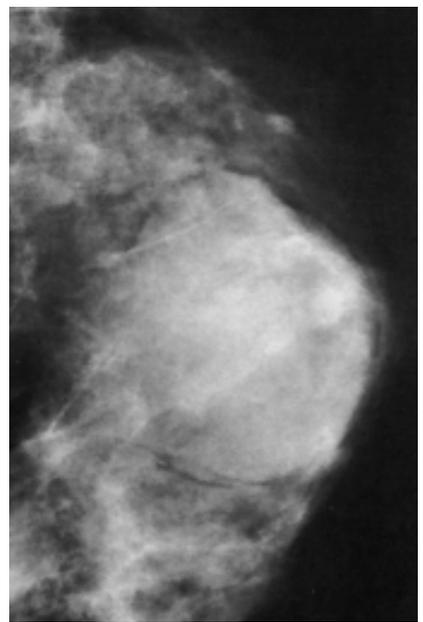


Figure 4. Circumscribed Mass. This is a simple cyst. Notice the dark halo around the cyst which is also a benign sign.

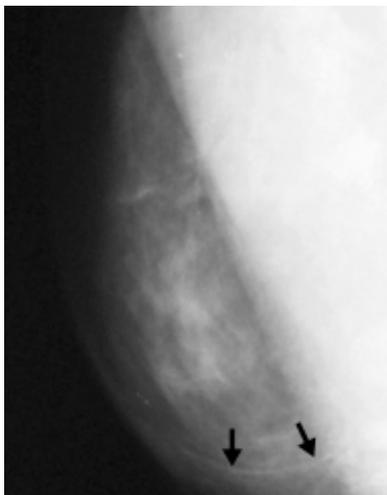


Figure 5. Lipoma. The arrows point to the capsule sign, which indicate fat both inside and outside the lesion.

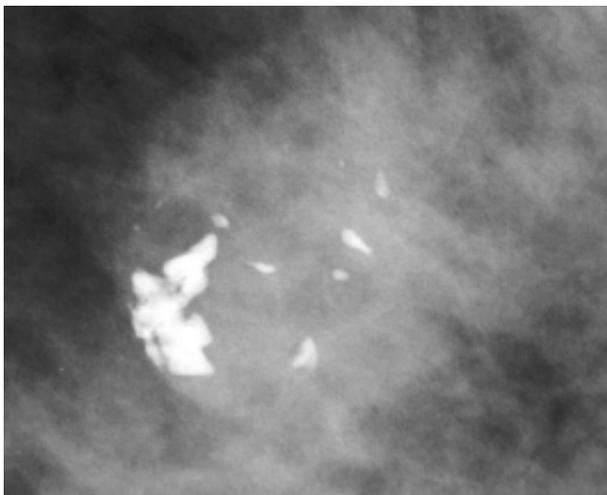


Figure 6. Coarse Calcification. This is a case of fibroadenoma.

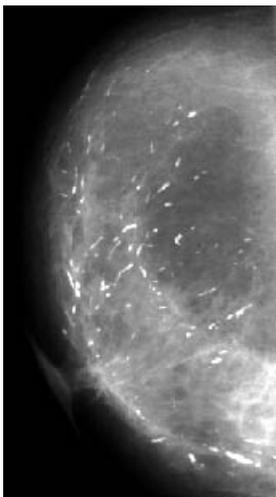


Figure 7. Large Rod-like Calcifications. This is a case of plasma cell mastitis. The calcifications are coarse, dense and rod like. They are ductal and periductal in origin.



Figure 8. Round Calcifications.

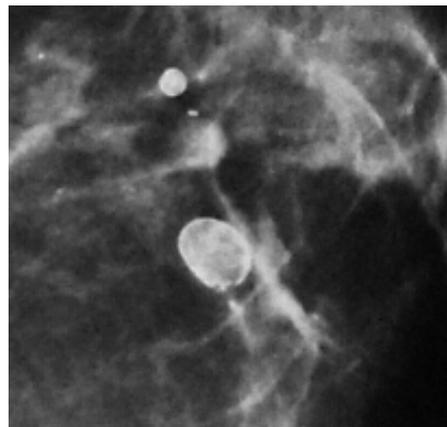


Figure 9. Lucent Centered Calcification.

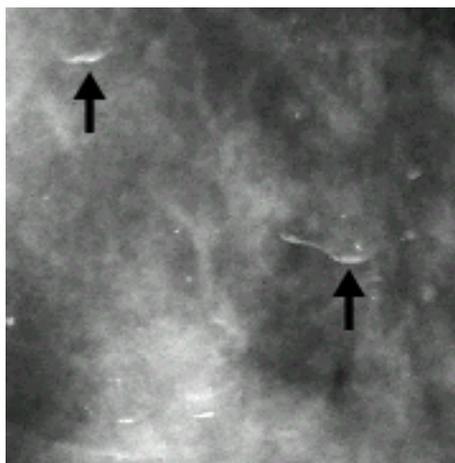


Figure 10. Sedimentation type of Calcification. Note the multiple calcium levels (arrows).

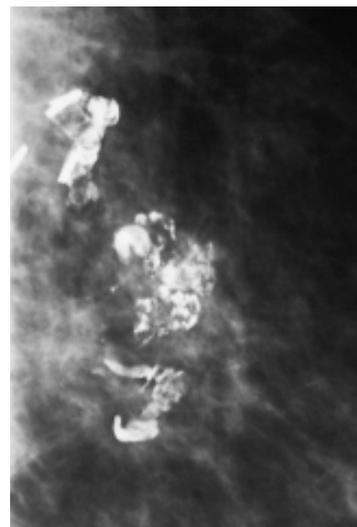


Figure 11. Suture and Dystrophic Calcifications.

Descriptions of calcification distribution include clustered, linear, segmental regional, diffuse/scattered and multiple. A segmental distribution (Figure 14) suggests that the calcifications lie within a duct and its branches. If associated with a not-typically benign morphology, malignancy has to be considered.

The Impression / Conclusion

The mammographic report usually ends with a conclusion and suggestion for further management. For negative and benign findings (Typically benign calcifications: e.g. sedimentation and fat containing lesions.), no further action is required.

For probably benign findings, short interval follow up would be suggested. For suspicious abnormalities, biopsy should be considered. For lesions highly suggestive of malignancy (spiculated masses, linear/branching calcifications) appropriate action should be taken.

It is hoped that the above discussion would give a basic approach to the reading of the mammogram and understanding of a mammographic report. Remember that the report is just one way of communication. For better management of the patient, one should discuss with the radiologists whenever in doubt. Also note that clinically detected (palpable) masses should be managed accordingly even if mammogram is negative.

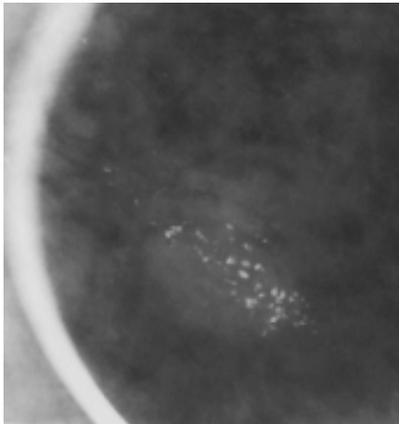


Figure 12. Granular Calcifications. The calcifications are clustered together. They vary in size, shape and density. This is a case of carcinoma.

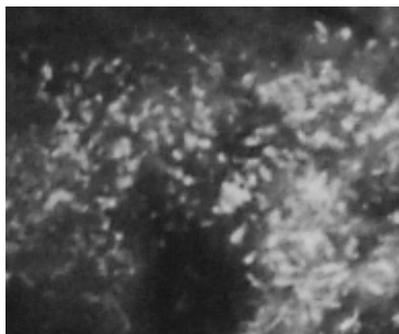


Figure 13. Casting Calcifications. This is a case of invasive ductal carcinoma. The calcifications are linear or branching. They are intraductal in location.

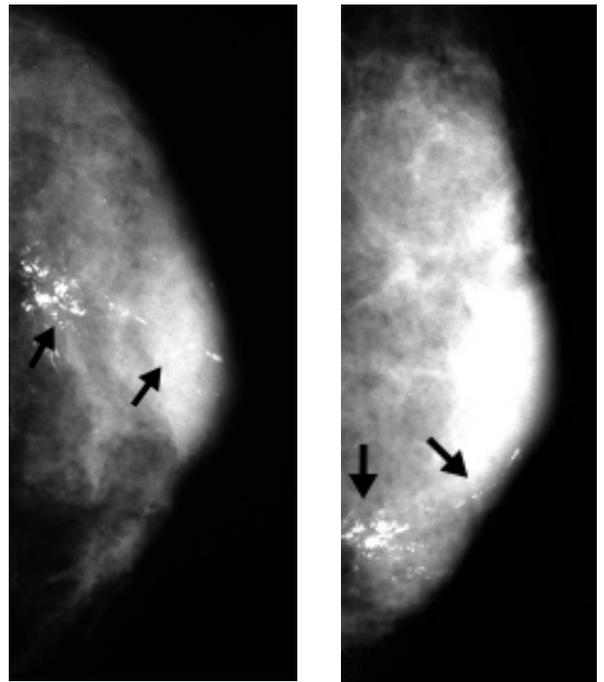


Figure 14. Segmental Distribution. This is a case with invasive ductal carcinoma. The arrows point to calcifications in a segmental distribution both in the CC and ML view. Also note that the calcifications extend along a duct towards the nipple.

Management of Gallstone in the Laparoscopic Era

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Introduction

Since the beginning of the early 90s, surgery has entered into what is known as the "laparoscopic era". Laparoscopic cholecystectomy (LC) is the first widely accepted procedure, and has clearly established as the standard operation for patients with gallstone disease for the past decade. The use of extra-corporeal shock wave lithotripsy (ESWL) has fallen out of favor since for a number of good reasons as follow:

- 1) Strict patient selection-criteria : Patient should have solitary radiolucent stone of <30 mm, or <3 non-calcified gallstones in a functioning gallbladder as demonstrated by an oral cholecystogram. More than one session might be required depending on the size and number of stones.
- 2) *Urso-deoxycholic acid*, the oral dissolution agent, has to be taken for a period of two years with uncertain success rate of complete stone clearance.
- 3) Even for patients with complete stone clearance, long-term follow-up study showed that one-third of them would have stone recurrence at 3 year.

Current Status of Laparoscopic Cholecystectomy

In the early half of the 90s, a number of randomized controlled trials were conducted to examine the relative values between LC and cholecystectomy via a mini-laparotomy (abdominal incision <10 cm). Different randomized controlled trials from the United Kingdom, Sweden unanimously supported the notion that LC offers patients a shorter hospital stay, less postoperative pain, reduced time for recuperation before returning to work. The less addressed issue is that LC offers also a superior cosmetic results, irrespective of the built of the patient. All these helped to popularized LC as the treatment of choice for patients with gallstone disease.

As a general guideline, the overall success rate of completing the procedure by LC is about 95%. The major cause for the conversion to open surgery remains to the difficulty of identifying the correct anatomy around the Carlot's triangle from repeated inflammatory attacks. Based on the experience of 500 LC at the Queen Mary Hospital, patient's age, degree of obesity, presence of

acute cholecystitis and the surgeon's experience were found to be important determinant. The risk of LC attracts a fair attention, especially in the early phase of its introduction as a new surgical procedure. In general, the mortality rate associated with LC is comparable with that of open cholecystectomy (0.02%). Although the gross complication rate remains at about 0.5% comparable to open cholecystectomy, most of the mishaps relate to bile duct injury of various extent. The more common forms of bile duct injuries encountered, at least in experienced hands, are either cystic duct stump leakage, or a pin-hole perforation of the bile duct from electric burn. If the injury is missed at the time of surgery, bile duct injury usually manifests itself clinically at about four days after surgery with rapidly progressive epigastric pain, and mildly deranged liver function tests. As these complications could usually be settled by a combined endoscopic and percutaneous drainage without resorting to open surgery, an acute awareness of the possibility is crucial to prevent further delay of appropriate treatment.

The usual hospital stay required after an elective LC ranged from 24 to 48 hours. There are advocates for pushing LC as a day-case procedure where patient was discharged on the evening after surgery. In a randomized study on 131 patients from South Australia, 18 percent of patients required hospitalization after surgery for nausea, vomiting or pain. Furthermore, there was no demonstrable reduction of cost at least in the Australasian setting.

Acute Cholecystitis

The indication of LC had been expanded with increasing experience. Although acute cholecystitis had been considered as a relative contra-indication for LC, recent studies confirmed that emergency LC, preferably within the first 72 hours after onset, is the appropriate operation given the necessary expertise is available. The increased technical complexity is best reflected by the high conversion rate to open surgery amongst patients subjected to emergency LC, which ranged from 11% to 20% as reported in the two randomized controlled trials, one from each of the university hospital in Hong Kong.

On the other hand, the conventional approach of treating the patient conservatively with antibiotic, allow the inflammation to subside over a period of 6 weeks, follow by an elective LC was proved to be an inferior option as "*delay*" treatment had resulted in (a) a substantial rate of failed conservative treatment (20%), (b) prolonged total hospital stay, and (c) a higher conversion rate to open surgery than "*emergency*" surgery.

On the technical side, emergency LC for acute cholecystitis is a more demanding operation. The operating time increased from the usual 60 minute for an elective case, to somewhere around 90 to 120 minutes is not unusual. Technical modifications are often necessary and drainage to the sub-hepatic space is often required for the increased oozing from the gallbladder bed, and the amount of saline used for irrigation during surgery. Together with the compromised gut function from the acute inflammation, the postoperative stay is often 3 to 4 days.

Technical Refinement

As reduction of postoperative pain and the superior cosmetic results lead to the popularity of LC, further improvements are geared these goals. The classical surgical technique for LC is a 4-ports approach. A 10-mm sub-umbilical port is mandatory as the 10-mm laparoscope is necessary to provide the optimal resolution and illumination for a safe operation, and the wound is the exit site for the operative specimen. Three additional ports are placed along the right sub-costal margin: the sub-xiphoid port (10 mm) for the usual instrumentations and most important of all, application of titanium clips to secure both the cystic duct and cystic artery, mid-clavicular port (5 mm) for retraction of the Hartmann's pouch to expose properly the crucial

anatomy at the Carlot's triangle, and the anterior axillary port (5 mm) for lifting the gallbladder by grasping its fundus. Most surgeons would operate alone with two hands holding instruments passed down from the sub-xiphoid and mid-axillary ports.

On approach to refine the results of LC is the reduction of the *number* of ports under the right sub-costal margin. Using a telescope which incorporates the optical lens and a working channel, LC could be accomplished with only one sub-costal port.

The alternative approach focuses on reduction on the size of surgical instruments used by using so-called "needlescopic" instruments of 3 mm or less in diameter. Technical modification becomes necessary as there is no commercially available clip applicator of such small diameter. The hurdle could be overcome by using knots either passed extra-corporeal or tied within the abdominal cavity. Such maneuvers could, however, be time-consuming and the better option would be using a mini-laparoscope to guide standard-size clips from the sub-umbilical port. The potential drawback is the inferior optical resolution and illumination and the best compromise is perhaps, the 3-mm mini-laparoscope using the Hopkins rod-lens system. In a personal series of 123 patients, the success rate of finishing the procedure with needlescopic instruments is over 80 percent and the comparable operating time is comparable with that of standard 5 and 10-mm instruments. While the ability to reduce postoperative pain from data obtained from randomized studies is conflicting, the cosmetic result achieved is the best possible. Needlescopic cholecystectomy is currently offered to all comers as the initial intent procedure except for patients with severe acute cholecystitis.